

### Question 1 of 247

A 34-year-old woman is admitted to the Emergency Department following a collapse. An ECG shows a polymorphic ventricular tachycardia. Which one of the following is not associated with an increased risk of developing torsade de pointes?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Tricyclic antidepressants |
| <input type="radio"/> | B. Subarachnoid haemorrhage  |
| <input type="radio"/> | C. Hypercalcaemia            |
| <input type="radio"/> | D. Romano-Ward syndrome      |
| <input type="radio"/> | E. Hypothermia               |

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Hypocalcaemia, not hypercalcaemia, causes prolongation of the QT interval and hence may predispose to the development of torsade de pointes

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"><li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li><li>Romano-Ward syndrome (no deafness)</li></ul>	<ul style="list-style-type: none"><li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li><li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li><li>methadone</li><li>chloroquine</li><li>terfenadine**</li><li>erythromycin</li></ul>	<ul style="list-style-type: none"><li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li><li>acute myocardial infarction</li><li>myocarditis</li><li>hypothermia</li><li>subarachnoid haemorrhage</li></ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest

- sudden cardiac death

## Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

### Question 2 of 247

A 54-year-old man is admitted to the Emergency Department with a 15 minute history of crushing central chest pain. Which one of the following rises first following a myocardial infarction?

- ☐ A. AST
- ☐ B. Troponin I
- ☐ C. CK
- ☐ D. CK-MB
- ☐ E. Myoglobin

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Myoglobin rises first following a myocardial infarction

### Cardiac enzymes and protein markers

Interpretation of the various cardiac enzymes has now largely been superseded by the introduction of troponin T and I. Questions still however commonly appear in the MRCP

Key points for the exam

- myoglobin is the first to rise
- CK-MB is useful to look for reinfarction as it returns to normal after 2-3 days (troponin T remains elevated for up to 10 days)

	Begins to rise	Peak value	Returns to normal
<b>Myoglobin</b>	1-2 hours	6-8 hours	1-2 days
<b>CK-MB</b>	2-6 hours	16-20 hours	2-3 days
<b>CK</b>	4-8 hours	16-24 hours	3-4 days
<b>Trop T</b>	4-6 hours	12-24 hours	7-10 days
<b>AST</b>	12-24 hours	36-48 hours	3-4 days
<b>LDH</b>	24-48 hours	72 hours	8-10 days

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### Question 3 of 247

A 17-year-old girl is brought into resus in cardiac arrest. On admission she is in asystole and attempts to resuscitate are unsuccessful. She collapsed whilst competing in a 1,500m race at college. The only past medical of note was asthma for which she occasionally used a salbutamol inhaler. There is no relevant family history. What is the most likely underlying cause of death?

- |                                  |  |
|----------------------------------|--|
| <input type="radio"/>            | A. Long QT syndrome                                      |
| <input checked="" type="radio"/> | B. Hypertrophic obstructive cardiomyopathy               |
| <input type="radio"/>            | C. Catecholaminergic polymorphic ventricular tachycardia |
| <input type="radio"/>            | D. Brugada syndrome                                      |
| <input type="radio"/>            | E. Arrhythmogenic right ventricular dysplasia            |

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HOCM is the most common cause of sudden cardiac death in the young

Hypertrophic obstructive cardiomyopathy (HOCM) is a more common cause of sudden cardiac death than arrhythmogenic right ventricular dysplasia (ARVD).

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a form of inherited cardiac disease which is also associated with sudden cardiac death. It is inherited in an autosomal dominant fashion and has a prevalence of around 1:10,000.

Brugada syndrome is a form of inherited cardiovascular disease which again may present with sudden cardiac death. It is inherited in an autosomal dominant fashion and has an estimated prevalence of 1:5,000-10,000. Brugada syndrome is more common in Asians.

#### HOCM: features

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

#### Features

- often asymptomatic
- dyspnoea, angina, syncope
- sudden death (most commonly due to ventricular arrhythmias), arrhythmias, heart failure
- jerky pulse, large 'a' waves, double apex beat
- ejection systolic murmur: increases with Valsalva manoeuvre and decreases on squatting

#### Associations



- Friedreich's ataxia
- Wolff-Parkinson White

Echo - mnemonic - MR SAM ASH

- mitral regurgitation (MR)
- systolic anterior motion (SAM) of the anterior mitral valve leaflet
- asymmetric hypertrophy (ASH)

ECG

- left ventricular hypertrophy
- progressive T wave inversion
- deep Q waves
- atrial fibrillation may occasionally be seen

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#### Question 4 of 247

A 54-year-old male with no past medical history is found to be in atrial fibrillation during a consultation regarding a sprained ankle. He reports no history of palpitations or dyspnoea. After discussing treatment options he elects not to be cardioverted. According to the latest European Society of Cardiology guidelines, if the patient remains in chronic atrial fibrillation what is the most suitable treatment to offer?

- ☐ A. Offer no treatment or low-dose aspirin. No treatment is the preferred option
- ☐ B. Warfarin
- ☐ C. Dabigatran
- ☐ D. Aspirin + dipyridamole
- ☐ E. Offer warfarin or low-dose aspirin. Aspirin is the preferred option

Young man with AF, no TIA or risk factors, no treatment is now preferred to aspirin

The European Society of Cardiology guidelines suggest that 'no treatment is preferred to aspirin' for low risk patients such as this man.

#### Atrial fibrillation: anticoagulation

The European Society of Cardiology published updated guidelines on the management of atrial fibrillation in 2012. They suggest using the **CHA<sub>2</sub>DS<sub>2</sub>-VASc** score to determine the most appropriate anticoagulation strategy. This scoring system superseded the CHADS<sub>2</sub>score.

	Condition	Points
<b>C</b>	Congestive heart failure	1
<b>H</b>	Hypertension (or treated hypertension)	1
<b>A<sub>2</sub></b>	Age $\geq$ 75 years	2
<b>D</b>	Diabetes	1
<b>S<sub>2</sub></b>	Prior Stroke or TIA	2
<b>V</b>	Vascular disease (including ischaemic heart disease and peripheral arterial disease)	1
<b>A</b>	Age 65-74 years	1
<b>S</b>	Sex (female)	1

The table below shows a suggested anticoagulation strategy\* based on the score:

Score	Anticoagulation
0	No treatment is preferred to aspirin
1	Oral anticoagulants preferred to aspirin; dabigatran is an alternative
2 or more	Oral anticoagulants; dabigatran is an alternative

\*the wording in the guidelines ('is preferred to') can be slightly confusing. It basically means that, say for a score of 0, whilst aspirin is an acceptable management option the weight of the clinical evidence would support no treatment instead

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### Question 5 of 247

A 54-year-old man is admitted following a myocardial infarction associated with ST elevation. He is treated with thrombolysis and does not undergo angioplasty. What advice should he be given regarding driving?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Can continue driving but must inform DVLA   |
| <input type="radio"/> | B. Cannot drive until an angiogram has been performed and reviewed by a cardiologist |
| <input type="radio"/> | C. Cannot drive for 1 week   |
| <input type="radio"/> | D. Cannot drive for 4 weeks  |
| <input type="radio"/> | E. Cannot drive for 12 weeks   |

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DVLA advice post MI - cannot drive for 4 weeks

### DVLA: cardiovascular disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

#### Specific rules

- hypertension - can drive unless treatment causes unacceptable side effects, no need to notify DVLA. If Group 2 Entitlement the disqualifies from driving if resting BP consistently 180 mmHg systolic or more and/or 100 mm Hg diastolic or more
- angioplasty (elective) - 1 week off driving
- CABG - 4 weeks off driving
- acute coronary syndrome- 4 weeks off driving, 1 week if successfully treated by angioplasty
- angina - driving must cease if symptoms occur at rest/at the wheel
- pacemaker insertion - 1 week off driving
- implantable cardioverter-defibrillator: if implanted for sustained ventricular arrhythmia: cease driving for 6 months. If implanted prophylactically then cease driving for 1 month
- successful catheter ablation for an arrhythmia- 2 days off driving
- aortic aneurysm of 6cm or more - notify DVLA. Licensing will be permitted subject to annual review. An aortic diameter of 6.5 cm or more disqualifies patients from driving
- heart transplant: DVLA do not need to be notified

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### Question 6 of 247

A 62-year-old man is admitted with to the cardiology ward with infective endocarditis. Blood cultures grow *Streptococcus bovis*. What is the most appropriate investigation given the blood culture findings?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Small bowel meal |
| <input type="radio"/> | B. Bronchoscopy     |
| <input type="radio"/> | C. Cystoscopy       |
| <input type="radio"/> | D. Gastroscopy      |
| <input type="radio"/> | E. Colonoscopy      |

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*Streptococcus bovis* endocarditis is associated with colorectal cancer

### Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. The following types of patients are affected:

- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

#### Causes

- *Streptococcus viridans* (most common cause - 40-50%)
- *Staphylococcus epidermidis* (especially prosthetic valves)
- *Staphylococcus aureus* (especially acute presentation, IVDUs)
- *Streptococcus bovis* is associated with colorectal cancer
- non-infective: systemic lupus erythematosus (Libman-Sacks), malignancy: marantic endocarditis

#### Culture negative causes

- prior antibiotic therapy
- *Coxiella burnetii*
- *Bartonella*
- *Brucella*
- HACEK: *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, *Kingella*)

Following prosthetic valve surgery *Staphylococcus epidermidis* is the most common organism in the first 2 months and is usually the result of perioperative contamination. After 2 months the spectrum of organisms which cause endocarditis return to normal, except with a slight increase in *Staph. aureus* infections

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### Question 7 of 247

A 65-year-old man with a history of paroxysmal atrial fibrillation presents with palpitations. He has no other history of note and a recent echocardiogram was normal. An ECG confirms fast atrial fibrillation. Which one of the following agents is most likely to cardiovert him into sinus rhythm?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Atenolol     |
| <input type="radio"/> | B. Procainamide |
| <input type="radio"/> | C. Flecainide   |
| <input type="radio"/> | D. Disopyramide |
| <input type="radio"/> | E. Digoxin      |

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Atrial fibrillation - cardioversion: amiodarone + flecainide

### Atrial fibrillation: pharmacological cardioversion

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines

Agents with proven efficacy in the pharmacological cardioversion of atrial fibrillation

- amiodarone
- flecainide (if no structural heart disease)
- others (less commonly used in UK): quinidine, dofetilide, ibutilide, propafenone

Less effective agents

- beta-blockers (including sotalol)
- calcium channel blockers
- digoxin
- disopyramide
- procainamide

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### Question 8 of 247

A 2-day-old baby girl is noted to become cyanotic whilst feeding and crying. A diagnosis of congenital heart disease is suspected. What is the most likely cause?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Transposition of the great arteries |
| <input type="radio"/> | B. Coarctation of the aorta            |
| <input type="radio"/> | C. Patent ductus arteriosus            |
| <input type="radio"/> | D. Tetralogy of Fallot                 |
| <input type="radio"/> | E. Ventricular septal defect           |

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#### Congenital heart disease

- cyanotic: TGA most common at birth, Fallot's most common overall
- acyanotic: VSD most common cause

The key point to this question is that whilst tetralogy of Fallot is more common than transposition of the great arteries (TGA), Fallot's doesn't usually present until 1-2 months following the identification of a murmur or cyanosis. In the neonate, TGA is the most common presenting cause of cyanotic congenital heart disease. The other 3 options are causes of acyanotic congenital heart disease.

#### Congenital heart disease: types

##### Acyanotic - most common causes

- ventricular septal defects (VSD) - most common, accounts for 30%
- atrial septal defect (ASD)
- patent ductus arteriosus (PDA)
- coarctation of the aorta
- aortic valve stenosis

VSDs are more common than ASDs. However, in adult patients ASDs are the more common new diagnosis as they generally present later.

##### Cyanotic - most common causes

- tetralogy of Fallot
- transposition of the great arteries (TGA)
- tricuspid atresia
- pulmonary valve stenosis



Fallot's is more common than TGA. However, at birth TGA is the more common lesion as patients with Fallot's generally presenting at around 1-2 months

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### Question 9 of 247

A 26-year-old female is admitted to hospital with palpitations. ECG shows a shortened PR interval and wide QRS complexes associated with a slurred upstroke seen in lead II. What is the definitive management of this condition?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Accessory pathway ablation |
| <input type="radio"/> | B. Lifelong aspirin           |
| <input type="radio"/> | C. AV node ablation           |
| <input type="radio"/> | D. Lifelong amiodarone        |
| <input type="radio"/> | E. Permanent pacemaker        |

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This patient has Wolff-Parkinson White syndrome, with accessory pathway ablation being the definitive treatment.

### Wolff-Parkinson White

Wolff-Parkinson White (WPW) syndrome is caused by a congenital accessory conducting pathway between the atria and ventricles leading to a atrioventricular re-entry tachycardia (AVRT). As the accessory pathway does not slow conduction AF can degenerate rapidly to VF

Possible ECG features include:

- short PR interval
- wide QRS complexes with a slurred upstroke - 'delta wave'
- left axis deviation if right-sided accessory pathway\*
- right axis deviation if left-sided accessory pathway\*

Differentiating between type A and type B

- type A (left-sided pathway): dominant R wave in V1
- type B (right-sided pathway): no dominant R wave in V1

Associations of WPW

- HOCM
- mitral valve prolapse
- Ebstein's anomaly
- thyrotoxicosis
- secundum ASD

## Management

- definitive treatment: radiofrequency ablation of the accessory pathway
- medical therapy: sotalol\*\*, amiodarone, flecainide

\*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

\*\*sotalol should be avoided if there is coexistent atrial fibrillation as prolonging the refractory period at the AV node may increase the rate of transmission through the accessory pathway, increasing the ventricular rate and potentially deteriorating into ventricular fibrillation

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A 71-year-old woman is reviewed in the falls clinic. Her blood pressure is 146/ 94 mmHg. This is confirmed on a second reading. In line with recent NICE guidance, what is the most appropriate next-step?

- ☐ A. Ask her to come back in 6 months for a blood pressure check
- ☐ B. Arrange 3 blood pressure checks with the practice nurse over the next 2 weeks with medical review following
- ☐ C. Arrange ambulatory blood pressure monitoring
- ☐ D. Reassure her this is acceptable for her age
- ☐ E. Start treatment with a calcium channel blocker

Next question

Hypertension - NICE now recommend ambulatory blood pressure monitoring to aid diagnosis

The 2011 NICE guidelines recognise that in the past there was overtreatment of 'white coat' hypertension. The use of ambulatory blood pressure monitoring (ABPM) aims to reduce this. There is also good evidence that ABPM is a better predictor of cardiovascular risk than clinic blood pressure readings. See the following study for more details:

*Verdecchia P. Prognostic value of ambulatory blood pressure: current evidence and clinical implications. Hypertension 2000; 35: 844-851*

### Hypertension: diagnosis and management

NICE published updated guidelines for the management of hypertension in 2011. Some of the key changes include:

- classifying hypertension into stages
- recommending the use of ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM)
- calcium channel blockers are now considered superior to thiazides
- bendroflumethiazide is no longer the thiazide of choice

### Blood pressure classification

This becomes relevant later in some of the management decisions that NICE advocate.

<b>Stage 1 hypertension</b>	Clinic BP $\geq$ 140/90 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 135/85 mmHg
<b>Stage 2 hypertension</b>	Clinic BP $\geq$ 160/100 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 150/95 mmHg
<b>Severe hypertension</b>	Clinic systolic BP $\geq$ 180 mmHg, or clinic diastolic BP $\geq$ 110 mmHg

## Diagnosing hypertension

If a BP reading is  $\geq 140 / 90$  mmHg patients should be offered ABPM to confirm the diagnosis.

Patients with a BP reading of  $\geq 180/110$  mmHg should be considered for immediate treatment.

Ambulatory blood pressure monitoring (ABPM)

- at least 2 measurements per hour during the person's usual waking hours (for example, between 08:00 and 22:00)
- use the average value of at least 14 measurements

If ABPM is not tolerated or declined HBPM should be offered.

Home blood pressure monitoring (HBPM)

- for each BP recording, two consecutive measurements need to be taken, at least 1 minute apart and with the person seated
- BP should be recorded twice daily, ideally in the morning and evening
- BP should be recorded for at least 4 days, ideally for 7 days
- discard the measurements taken on the first day and use the average value of all the remaining measurements

## Managing hypertension

ABPM/HBPM  $\geq 135/85$  mmHg (i.e. stage 1 hypertension)

- treat if  $< 80$  years of age and any of the following apply; target organ damage, established cardiovascular disease, renal disease, diabetes or a 10-year cardiovascular risk equivalent to 20% or greater

ABPM/HBPM  $\geq 150/95$  mmHg (i.e. stage 2 hypertension)

- offer drug treatment regardless of age

For patients  $< 40$  years consider specialist referral to exclude secondary causes.

Step 1 treatment

- patients  $< 55$ -years-old: ACE inhibitor (A)
- patients  $> 55$ -years-old or of Afro-Caribbean origin: calcium channel blocker

Step 2 treatment

- ACE inhibitor + calcium channel blocker (A + C)

### Step 3 treatment

- add a thiazide diuretic (D, i.e. A + C + D)
- NICE now advocate using either chlorthalidone (12.5-25.0 mg once daily) or indapamide (1.5 mg modified-release once daily or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide

NICE define a clinic BP  $\geq 140/90$  mmHg after step 3 treatment with optimal or best tolerated doses as resistant hypertension. They suggest step 4 treatment or seeking expert advice

### Step 4 treatment

- consider further diuretic treatment
- if potassium  $< 4.5$  mmol/l add spironolactone 25mg od
- if potassium  $> 4.5$  mmol/l add higher-dose thiazide-like diuretic treatment
- if further diuretic therapy is not tolerated, or is contraindicated or ineffective, consider an alpha- or beta-blocker

If BP still not controlled seek specialist advice.

### Blood pressure targets

	Clinic BP	ABPM / HBPM
Age $< 80$ years	140/90 mmHg	135/85 mmHg
Age $> 80$ years	150/90 mmHg	145/85 mmHg

### New drugs

#### Direct renin inhibitors

- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

### Question 11 of 247

A 74-year-old woman is reviewed. She recently had ambulatory blood pressure monitoring that showed an average reading of 142/90 mmHg. There is no significant past medical history of note other than hypothyroidism. Her 10-year cardiovascular risk score is 23%. What is the most appropriate management?

- ☐ A. Start amlodipine
- ☐ B. Start bendroflumethiazide
- ☐ C. No treatment required - monitor blood pressure every year
- ☐ D. Start ramipril
- ☐ E. Repeat ambulatory blood pressure monitoring

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The average reading is above the treatment threshold for patients below the age of 80 years. Treatment with a calcium channel blocker should therefore be started.

### Hypertension: diagnosis and management

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## Managing hypertension

ABPM/HBPM  $\geq$  135/85 mmHg (i.e. stage 1 hypertension)

- treat if  $<$  80 years of age and any of the following apply; target organ damage, established cardiovascular disease, renal disease, diabetes or a 10-year cardiovascular risk equivalent to 20% or greater

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Step 2 treatment

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- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

### Question 12 of 247

You review a 62-year-old man who has recently been discharged from hospital in Hungary following a myocardial infarction. He brings a copy of an echocardiogram report which shows his left ventricular ejection fraction is 48%. On examination his pulse is 78 / min and regular, blood pressure is 124 / 72 mmHg and his chest is clear. His current medications include aspirin, simvastatin and lisinopril. What is the most appropriate next step in terms of his medication?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Add atenolol               |
| <input type="radio"/> | B. Add furosemide             |
| <input type="radio"/> | C. Add bisoprolol             |
| <input type="radio"/> | D. Add isosorbide mononitrate |
| <input type="radio"/> | E. Make no changes            |

Both carvedilol and bisoprolol have been shown to reduce mortality in stable heart failure. The other beta-blockers have no evidence base to support their use.

NICE recommend that all heart failure patients should take both an ACE-inhibitor and a beta-blocker.

#### Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:

- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:

- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin\* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off\*\* pneumococcal vaccine

\*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

\*\*adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years

A 55-year-old man is admitted to the Emergency Department with 'tearing' chest pain radiating through to his back. Examination reveals a pulse of 96 / min regular, blood pressure of 130/85 mmHg and oxygen saturations of 97% on room air. A chest x-ray shows mediastinal widening. A CT shows dissection of the ascending aorta. What is the most suitable initial management?

- |                                  |                            |
|----------------------------------|----------------------------|
| <input type="radio"/>            | A. IV sodium nitroprusside |
| <input type="radio"/>            | B. Oral verapamil          |
| <input type="radio"/>            | C. Observe only            |
| <input checked="" type="radio"/> | D. IV labetalol            |
| <input type="radio"/>            | E. Surgical repair         |

Next question

#### Aortic dissection

- type A - ascending aorta - control BP(IV labetalol) + surgery
- type B - descending aorta - control BP(IV labetalol)

The question tests ability to apply textbook knowledge to real world situations. Whilst surgical referral should be made as soon as possible definite surgery will inevitably take time and the blood pressure should be controlled in the meantime

#### Aortic dissection: management

##### Stanford classification

- type A - ascending aorta, 2/3 of cases
- type B - descending aorta, distal to left subclavian origin, 1/3 of cases

##### DeBakey classification

- type I - originates in ascending aorta, propagates to at least the aortic arch and possibly beyond it distally
- type II - originates in and is confined to the ascending aorta
- type III - originates in descending aorta, rarely extends proximally but will extend distally

##### Type A

- surgical management, but blood pressure should be controlled to a target systolic of 100-120 mmHg whilst awaiting intervention

## Type B\*

- conservative management
- bed rest
- reduce blood pressure IV labetalol to prevent progression

\*endovascular repair of type B aortic dissection may have a role in the future

Next

### Question 14 of 247

A 72-year-old man presents with lethargy and palpitations for the past four or five days. On examination his pulse is 123 bpm irregularly irregular, blood pressure is 118/70 mmHg and his chest is clear. An ECG confirms atrial fibrillation. What is the appropriate drug to control his heart rate?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Amiodarone |
| <input type="radio"/> | B. Atenolol   |
| <input type="radio"/> | C. Digoxin    |
| <input type="radio"/> | D. Amlodipine |
| <input type="radio"/> | E. Flecainide |

[Next question](#)

Atrial fibrillation: rate control - beta blockers preferable to digoxin

A number of factors including age and symptoms would favour a rate control strategy. The NICE guidelines suggest either a beta-blocker or a rate limiting calcium channel blocker (i.e. Not amlodipine) in this situation. Some clinicians would prefer to use a more cardio-selective beta-blocker such as bisoprolol, although this is not stipulated in current guidelines

#### Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
Older than 65 years History of ischaemic heart disease	Younger than 65 years Symptomatic First presentation Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) Congestive heart failure

Next

### Question 15 of 247

A 17-year-old female presents with recurrent attacks of collapse. These episodes typically occur without warning and have occurred whilst she was running for a bus. There is no significant past medical history and the only family history of note is that her father died suddenly when he was 38-years-old. What is the likely cause?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Vaso-vagal attacks  |
| <input type="radio"/> | B. Anxiety             |
| <input type="radio"/> | C. Epilepsy            |
| <input type="radio"/> | D. Cardiogenic syncope |
| <input type="radio"/> | E. Malingering         |

[Next question](#)

Sudden death, unusual collapse in young person - ? HOCM

This is a rather vague question. However, a family history of sudden death should make you think of conditions such as hypertrophic obstructive cardiomyopathy

#### HOCM: features

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

#### Features

- often asymptomatic
- dyspnoea, angina, syncope
- sudden death (most commonly due to ventricular arrhythmias), arrhythmias, heart failure
- jerky pulse, large 'a' waves, double apex beat
- ejection systolic murmur: increases with Valsalva manoeuvre and decreases on squatting

#### Associations

- Friedreich's ataxia
- Wolff-Parkinson White

#### Echo - mnemonic - MR SAM ASH

- mitral regurgitation (MR)
- systolic anterior motion (SAM) of the anterior mitral valve leaflet
- asymmetric hypertrophy (ASH)

## ECG

- left ventricular hypertrophy
- progressive T wave inversion
- deep Q waves
- atrial fibrillation may occasionally be seen

Next



### Question 16 of 247

A 52-year-old man is seen in the hypertension clinic. He was diagnosed around three months ago and started on ramipril. This has been titrated up to 10mg od but his blood pressure remains around 156/92 mmHg. What is the most appropriate next step in management?

- ☐ A. Add bendroflumethiazide
- ☐ B. Add bisoprolol
- ☐ C. Switch ramipril to perindopril
- ☐ D. Add amlodipine
- ☐ E. Add losartan

[Next question](#)

Calcium channel blockers are now preferred to thiazides in the treatment of hypertension

The 2011 NICE guidelines reflected the changing evidence base supporting the use of calcium channel blockers in preference to thiazide-type diuretics in the management of hypertension.

### Hypertension: diagnosis and management

NICE published updated guidelines for the management of hypertension in 2011. Some of the key changes include:

- classifying hypertension into stages
- recommending the use of ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM)
- calcium channel blockers are now considered superior to thiazides
- bendroflumethiazide is no longer the thiazide of choice

### Blood pressure classification

This becomes relevant later in some of the management decisions that NICE advocate.

<b>Stage 1 hypertension</b>	Clinic BP $\geq$ 140/90 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 135/85 mmHg
<b>Stage 2 hypertension</b>	Clinic BP $\geq$ 160/100 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 150/95 mmHg
<b>Severe hypertension</b>	Clinic systolic BP $\geq$ 180 mmHg, or clinic diastolic BP $\geq$ 110 mmHg

### Diagnosing hypertension

If a BP reading is  $\geq$  140 / 90 mmHg patients should be offered ABPM to confirm the diagnosis.

Patients with a BP reading of  $\geq 180/110$  mmHg should be considered for immediate treatment.

#### Ambulatory blood pressure monitoring (ABPM)

- at least 2 measurements per hour during the person's usual waking hours (for example, between 08:00 and 22:00)
- use the average value of at least 14 measurements

If ABPM is not tolerated or declined HBPM should be offered.

#### Home blood pressure monitoring (HBPM)

- for each BP recording, two consecutive measurements need to be taken, at least 1 minute apart and with the person seated
- BP should be recorded twice daily, ideally in the morning and evening
- BP should be recorded for at least 4 days, ideally for 7 days
- discard the measurements taken on the first day and use the average value of all the remaining measurements

### Managing hypertension

ABPM/HBPM  $\geq 135/85$  mmHg (i.e. stage 1 hypertension)

- treat if  $< 80$  years of age and any of the following apply; target organ damage, established cardiovascular disease, renal disease, diabetes or a 10-year cardiovascular risk equivalent to 20% or greater

ABPM/HBPM  $\geq 150/95$  mmHg (i.e. stage 2 hypertension)

- offer drug treatment regardless of age

For patients  $< 40$  years consider specialist referral to exclude secondary causes.

#### Step 1 treatment

- patients  $< 55$ -years-old: ACE inhibitor (A)
- patients  $> 55$ -years-old or of Afro-Caribbean origin: calcium channel blocker

#### Step 2 treatment

- ACE inhibitor + calcium channel blocker (A + C)

#### Step 3 treatment

- add a thiazide diuretic (D, i.e. A + C + D)
- NICE now advocate using either chlorthalidone (12.5-25.0 mg once daily) or indapamide (1.5 mg modified-release once daily or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide

NICE define a clinic BP  $\geq 140/90$  mmHg after step 3 treatment with optimal or best tolerated doses as resistant hypertension. They suggest step 4 treatment or seeking expert advice

#### Step 4 treatment

- consider further diuretic treatment
- if potassium  $< 4.5$  mmol/l add spironolactone 25mg od
- if potassium  $> 4.5$  mmol/l add higher-dose thiazide-like diuretic treatment
- if further diuretic therapy is not tolerated, or is contraindicated or ineffective, consider an alpha- or beta-blocker

If BP still not controlled seek specialist advice.

#### Blood pressure targets

	Clinic BP	ABPM / HBPM
Age $< 80$ years	140/90 mmHg	135/85 mmHg
Age $> 80$ years	150/90 mmHg	145/85 mmHg

#### New drugs

##### Direct renin inhibitors

- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

### Question 17 of 247

A 65-year-old man is found to have an ejection systolic murmur and narrow pulse pressure on examination. He has experienced no chest pain, breathlessness or syncope. An echo confirms aortic stenosis and shows an aortic valve gradient of 40 mmHg. How should this patient be managed?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Routine aortic valve replacement     |
| <input type="radio"/> | B. Urgent aortic valve replacement      |
| <input type="radio"/> | C. Anticoagulation                      |
| <input type="radio"/> | D. Aortic valvuloplasty                 |
| <input type="radio"/> | E. Regular cardiology outpatient review |

[Next question](#)

Aortic stenosis management: AVR if symptomatic, otherwise cut-off is gradient of 50 mmHg

No action should be taken at present as he is currently asymptomatic. If the aortic valve gradient > 50 mmHg or there is evidence of significant left ventricular dysfunction then surgery is sometimes considered in selected asymptomatic patients

### Aortic stenosis

Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis

- degenerative calcification (most common cause in older patients > 65 years)
- bicuspid aortic valve (most common cause in younger patients < 65 years)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management

- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient  $> 50$  mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Next

### Question 18 of 247

A 30-year-old woman presents to the Emergency Department with a one-day history of central chest pain. The pain is described as severe, non-radiating and eases on expiration. Clinical examination of her cardiorespiratory system is unremarkable other than a heart rate of 96 / min. An ECG shows widespread ST elevation in the anterior, inferior and lateral leads. Bloods show the following:

Full blood count	Normal
Urea and electrolytes	Normal
Troponin I	0.8 ng/mL (< 0.2 ng/mL)

What is the most likely diagnosis?

- ☐ A. Pulmonary embolism
- ☐ B. Acute coronary syndrome
- ☐ C. Hypertrophic obstructive cardiomyopathy
- ☐ D. Acute pericarditis
- ☐ E. Arrhythmogenic right ventricular cardiomyopathy

[Next question](#)

A modest rise in troponin is seen in around one-third of patients with acute pericarditis.

#### Pericarditis

Pericarditis is one of the differentials of any patient presenting with chest pain.

##### Features

- chest pain: may be pleuritic. Is often relieved by sitting forwards
- other symptoms include non-productive cough, dyspnoea and flu-like symptoms
- pericardial rub
- tachypnoea
- tachycardia

##### Causes

- viral infections (Coxsackie)
- tuberculosis
- uraemia (causes 'fibrinous' pericarditis)
- trauma
- post-myocardial infarction, Dressler's syndrome
- connective tissue disease
- hypothyroidism

## ECG changes

- widespread 'saddle-shaped' ST elevation
- PR depression

Next

### Question 19 of 247

A 58-year-old man with no past medical history of note is admitted to hospital with crushing central chest pain. ECG on arrival shows anterior ST elevation and he is subsequently thrombolysed with a good resolution of symptoms and ECG changes. Two months following discharge from hospital, which combination of drugs should he be taking?

- ☐ A. ACE inhibitor + beta-blocker + statin + aspirin
- ☐ B. Spironolactone + beta-blocker + statin + aspirin
- ☐ C. ACE inhibitor + beta-blocker + statin + aspirin + clopidogrel
- ☐ D. ACE inhibitor + statin + aspirin + clopidogrel
- ☐ E. Beta-blocker + statin + aspirin + clopidogrel

The current guidance is to continue clopidogrel for 4 weeks following a ST-elevation myocardial infarction

#### Myocardial infarction: secondary prevention

NICE produced guidelines on the management of patients following a myocardial infarction (MI) in 2007. Some key points are listed below

All patients should be offered the following drugs:

- ACE inhibitor
- beta-blocker
- aspirin
- statin

Clopidogrel

- ST-segment-elevation MI: patients treated with a combination of aspirin and clopidogrel during the first 24 hours after the MI should continue this treatment for at least 4 weeks
- non-ST segment elevation myocardial infarction (NSTEMI): following the 2010 NICE unstable angina and NSTEMI guidelines clopidogrel should be given for the first 12 months if the 6 month mortality risk\* is > 1.5%

Aldosterone antagonists

- patients who have had an acute MI and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, treatment with an aldosterone antagonist licensed for post-MI treatment (e.g. eplerenone) should be initiated within 3-14 days of the MI, preferably after ACE inhibitor therapy

\*this can be calculated using scoring systems such as GRACE



A 71-year-old man is reviewed in the coronary care unit. He was admitted with an anterior ST-elevation myocardial infarction and received thrombolysis with alteplase. Ninety minutes following this an ECG shows a 30-40% resolution in the ST elevation. What is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Percutaneous coronary intervention  |
| <input type="radio"/> | B. Repeat ECG in 4 hours, if still not a 50% resolution in ST elevation then proceed to percutaneous coronary intervention |
| <input type="radio"/> | C. Repeat thrombolysis with alteplase  |
| <input type="radio"/> | D. Start a nitrate infusion  |
| <input type="radio"/> | E. Inform his relatives that further intervention is futile and ensure adequate pain relief                                |

[Next question](#)

### Myocardial infarction: management

A number of studies over the past 10 years have provided an evidence for the management of ST-elevation myocardial infarction (STEMI)

In the absence of contraindications, all patients should be given

- aspirin
- clopidogrel: the two major studies (CLARITY and COMMIT) both confirmed benefit but used different loading doses (300mg and 75mg respectively)
- low molecular weight heparin

NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO<sub>2</sub>) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO<sub>2</sub> of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO<sub>2</sub> of 88-92% until blood gas analysis is available.

Primary percutaneous coronary intervention (PCI) has emerged as the gold-standard treatment for STEMI but is not available in all centres. Thrombolysis should be performed in patients without access to primary PCI

With regards to thrombolysis:

- tissue plasminogen activator (tPA) has been shown to offer clear mortality benefits over streptokinase
- tenecteplase is easier to administer and has been shown to have non-inferior efficacy to alteplase with a similar adverse effect profile

An ECG should be performed 90 minutes following thrombolysis to assess whether there has been a greater than 50% resolution in the ST elevation

- if there has not been adequate resolution then rescue PCI is superior to repeat thrombolysis
- for patients successfully treated with thrombolysis PCI has been shown to be beneficial. The optimal timing of this is still under investigation

**Question 21 of 247**

A 59-year-old female is admitted to the Emergency Department with a 30 minute history of central chest pain radiating to her left arm. An ECG shows ST elevation in leads II, III, aVF. Which coronary artery is most likely to be affected?

- ☐ A. Right coronary
- ☐ B. Left anterior descending
- ☐ C. Left main stem
- ☐ D. Left circumflex
- ☐ E. Anterior interventricular

[Next question](#)

Inferior MI - right coronary artery lesion

**ECG: coronary territories**

The table below shows the correlation between ECG changes and coronary territories:

	ECG changes	Coronary artery
<b>Anteroseptal</b>	V1-V4	Left anterior descending
<b>Inferior</b>	II, III, aVF	Right coronary
<b>Anterolateral</b>	V4-6, I, aVL	Left anterior descending or left circumflex
<b>Lateral</b>	I, aVL +/- V5-6	Left circumflex
<b>Posterior</b>	Tall R waves V1-2	Usually left circumflex, also right coronary

A 55-year-old smoker with a past history of hypertension presents to the Emergency Department with shortness-of-breath since the morning. Examination reveals bibasal crackles whilst the CXR shows upper lobe diversion and perihilar shadowing. The ECG and cardiac enzymes are normal. What is the likely cause of his breathlessness?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Infective endocarditis         |
| <input type="radio"/> | B. Pheochromocytoma               |
| <input type="radio"/> | C. Fibromuscular dysplasia        |
| <input type="radio"/> | D. Renal artery stenosis          |
| <input type="radio"/> | E. Anterior myocardial infarction |

Next question

Flash pulmonary oedema, U&Es worse on ACE inhibitor, asymmetrical kidneys --> renal artery stenosis - do MR angiography

Renal artery stenosis may cause sudden onset or 'flash' pulmonary oedema. A myocardial infarction is unlikely given the normal ECG and cardiac enzymes. Chest pain would also be expected in a 55-year-old patient with no history of diabetes. Fibromuscular dysplasia is generally seen in young woman

### Renal vascular disease

Renal vascular disease is most commonly due to atherosclerosis (> 95% of patients). It is associated with risk factors such as smoking and hypertension that cause atheroma elsewhere in the body. It may present as hypertension, chronic renal failure or 'flash' pulmonary oedema. In younger patients however fibromuscular dysplasia (FMD) needs to be considered. FMD is more common in young women and characteristically has a 'string of beads' appearance on angiography. Patients respond well to balloon angioplasty

#### Investigation

- MR angiography is now the investigation of choice
- CT angiography
- conventional renal angiography is less commonly performed used nowadays, but may still have a role when planning surgery

An 18-year-old female who is known to have Turner's syndrome is referred to cardiology as she has a murmur. On examination a soft ejection systolic murmur is heard. What is the most likely cause of this finding?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Coarctation of the aorta      |
| <input type="radio"/> | B. Ventricular septal defect     |
| <input type="radio"/> | C. Pulmonary stenosis            |
| <input type="radio"/> | D. Supravalvular aortic stenosis |
| <input type="radio"/> | E. Bicuspid aortic valve         |

[Next question](#)

Turner's syndrome - most common cardiac defect is bicuspid aortic valve

### Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

#### Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

A 74-year-old man presents for a medication review. Blood pressure is recorded as 184/72 mmHg. This is confirmed on two further occasions. What is the most appropriate first line therapy?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Ramipril            |
| <input type="radio"/> | B. Losartan            |
| <input type="radio"/> | C. Bendroflumethiazide |
| <input type="radio"/> | D. Amlodipine          |
| <input type="radio"/> | E. Atenolol            |

[Next question](#)

The 2011 NICE guidelines recommended treating isolated systolic hypertension the same way as standard hypertension. In this age group calcium channel blockers would be first-line.

### Isolated systolic hypertension

Isolated systolic hypertension (ISH) is common in the elderly, affecting around 50% of people older than 70 years old. The Systolic Hypertension in the Elderly Program (SHEP) back in 1991 established that treating ISH reduced both strokes and ischaemic heart disease. Drugs such as thiazides were recommended as first line agents. This approach is contradicted by the 2011 NICE guidelines which recommends treating ISH in the same stepwise fashion as standard hypertension.

Which one of the following is not an indication for insertion of a temporary pacemaker?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Complete heart block following an inferior MI - blood pressure normal       |
| <input type="radio"/> | B. Complete heart block following an anterior MI - blood pressure normal       |
| <input type="radio"/> | C. Trifascicular block prior to surgery  |
| <input type="radio"/> | D. Mobitz type II heart block following an anterior MI - blood pressure normal |
| <input type="radio"/> | E. Symptomatic bradycardia not responding to drug treatment                    |

Next question

Complete heart block following an inferior MI is NOT an indication for pacing, unlike with an anterior MI

Post-inferior MI complete heart block is common and can be managed conservatively if the patient is asymptomatic and haemodynamically stable

### **Pacemakers: temporary**

Indications for a temporary pacemaker

- symptomatic/haemodynamically unstable bradycardia, not responding to atropine
- post-ANTERIOR MI: type 2 or complete heart block\*
- trifascicular block prior to surgery

\*post-INFERIOR MI complete heart block is common and can be managed conservatively if asymptomatic and haemodynamically stable

Which one of the following treatments have not been shown to improve mortality in patients with chronic heart failure?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Beta-blockers            |
| <input type="radio"/> | B. Spironolactone           |
| <input type="radio"/> | C. Frusemide                |
| <input type="radio"/> | D. Nitrates and hydralazine |
| <input type="radio"/> | E. Enalapril                |

Next question

Whilst useful in managing the symptoms of acute and chronic heart failure frusemide offers no prognostic benefits.

### Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:

- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:

- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin\* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off\*\* pneumococcal vaccine

\*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

\*\*adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years



A 70-year-old woman is brought to the Emergency Department by her relatives. For the past two hours she has experienced palpitations and 'tightness' in her chest. An ECG taken on arrival shows baseline atrial activity of around 300/min with a ventricular rate of 150/min. What is the most likely diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Atrioventricular nodal re-entry tachycardia (AVNRT) |
| <input type="radio"/> | B. Atrial flutter                                      |
| <input type="radio"/> | C. Atrioventricular re-entry tachycardia (AVRT)        |
| <input type="radio"/> | D. Junctional tachycardia                              |
| <input type="radio"/> | E. Atrial fibrillation                                 |

[Next question](#)

Tachycardia with a rate of 150/min ?atrial flutter

### Atrial flutter

Atrial flutter is a form of supraventricular tachycardia characterised by a succession of rapid atrial depolarisation waves.

#### ECG findings

- 'sawtooth' appearance
- as the underlying atrial rate is often around 300/min the ventricular or heart rate is dependent on the degree of AV block. For example if there is 2:1 block the ventricular rate will be 150/min
- flutter waves may be visible following carotid sinus massage or adenosine

#### Management

- is similar to that of atrial fibrillation although medication may be less effective
- atrial flutter is more sensitive to cardioversion however so lower energy levels may be used
- radiofrequency ablation of the tricuspid valve isthmus is curative for most patients

You review a patient who has been admitted with a non-ST elevation myocardial infarction in the Emergency Department. Following recent NICE guidance, which patients should receive clopidogrel?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Those who have a predicted 6 month mortality > 1.5%                                       |
| <input type="radio"/> | B. Patients who have a history of hypertension, ischaemic heart disease or diabetes mellitus |
| <input type="radio"/> | C. Those who have a predicted 12 month mortality > 10%                                       |
| <input type="radio"/> | D. Those who have a predicted 6 month mortality < 10%  |
| <input type="radio"/> | E. All patients  |

[Next question](#)

NICE NSTEMI/unstable angina guidelines are based on 6 month mortality risk:

- if > 1.5% clopidogrel for 12 months
- if > 3% angiography within 96 hours

The 6 month mortality may be calculated using a validated risk model such as GRACE.

### Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive

- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

**Antithrombin** treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is > 265 µmol/l unfractionated heparin should be given.

**Clopidogrel** 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

**Coronary angiography** should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

<b>Aspirin</b>	Antiplatelet - inhibits the production of thromboxane A2
<b>Clopidogrel</b>	Antiplatelet - inhibits ADP binding to its platelet receptor
<b>Enoxaparin</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Fondaparinux</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Bivalirudin</b>	Reversible direct thrombin inhibitor

Next

### Question 29 of 247

Six weeks after having a prosthetic heart valve a patient develops infective endocarditis. What is the most likely causative organism?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. <i>Streptococcus viridans</i>     |
| <input type="radio"/> | B. <i>Staphylococcus epidermidis</i> |
| <input type="radio"/> | C. <i>Staphylococcus aureus</i>      |
| <input type="radio"/> | D. <i>Streptococcus bovis</i>        |
| <input type="radio"/> | E. One of the HACEK group            |

[Next question](#)

Most common cause of endocarditis:

- *Streptococcus viridans*
- *Staphylococcus epidermidis* if < 2 months post valve surgery

In the first two months following surgery for a prosthetic valve the most likely causative organism is *Staphylococcus epidermidis*

### Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. The following types of patients are affected:

- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

### Causes

- *Streptococcus viridans* (most common cause - 40-50%)
- *Staphylococcus epidermidis* (especially prosthetic valves)
- *Staphylococcus aureus* (especially acute presentation, IVDUs)
- *Streptococcus bovis* is associated with colorectal cancer
- non-infective: systemic lupus erythematosus (Libman-Sacks), malignancy: marantic endocarditis

### Culture negative causes

- prior antibiotic therapy
- *Coxiella burnetii*
- *Bartonella*
- *Brucella*
- HACEK: *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, *Kingella*)

Following prosthetic valve surgery *Staphylococcus epidermidis* is the most common organism in the first 2 months and is usually the result of perioperative contamination. After 2 months the spectrum of organisms which cause endocarditis return to normal, except with a slight increase in *Staph. aureus* infections

Next

### Question 30 of 247

A 60-year-old man presents with increasing shortness-of-breath on exertion. During the examination a third heart sound is heard. Examination of the respiratory system is unremarkable. Which one of the following is most consistent with this finding?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Dilated cardiomyopathy                  |
| <input type="radio"/> | B. Hypertrophic obstructive cardiomyopathy |
| <input type="radio"/> | C. Atrial fibrillation                     |
| <input type="radio"/> | D. Mitral stenosis                         |
| <input type="radio"/> | E. Normal variant                          |

A third heart sound is only considered a normal variant in patients < 40 years of age.

#### Heart sounds

The first heart sound (S1) is caused by closure of the mitral and tricuspid valves whilst the second heart sound (S2) is due to aortic and pulmonary valve closure

#### S1

- closure of mitral and tricuspid valves
- soft if long PR or mitral regurgitation
- loud in mitral stenosis

#### S2

- closure of aortic and pulmonary valves
- soft in aortic stenosis
- splitting during inspiration is normal

#### S3

- caused by diastolic filling of the ventricle
- considered normal if < 30 years old (may persist in women up to 50 years old)
- heard in left ventricular failure (e.g. dilated cardiomyopathy), constrictive pericarditis (called a pericardial knock)

#### S4

- may be heard in aortic stenosis, HOCM, hypertension
- caused by atrial contraction against a stiff ventricle
- in HOCM a double apical impulse may be felt as a result of a palpable S4

A 74-year-old man with symptomatic aortic stenosis is reviewed in the cardiology clinic. He is otherwise fit and well and keen for intervention if possible. What type of intervention is he most likely to be offered?

- ☐ A. Annual echocardiography, intervention when valve gradient > 75 mmHg
- ☐ B. Aortic bypass graft
- ☐ C. Bioprosthetic aortic valve replacement
- ☐ D. Balloon valvuloplasty
- ☐ E. Mechanical aortic valve replacement

Next question

Prosthetic heart valves - mechanical valves last longer and tend to be given to younger patients

### Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	Mechanical valves
Usually bovine or porcine in origin	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays
Major disadvantage is structural deterioration and calcification over time. Most older patients (> 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve	Mechanical valves have a low failure rate
Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication.
	Target INR <ul style="list-style-type: none"> <li>aortic: 2.0-3.0</li> <li>mitral: 2.5-3.5</li> </ul>

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.

A 36-year-old woman presents for a routine antenatal review. She is now 15 weeks pregnant. Her blood pressure in clinic is 154/94 mmHg. This is confirmed with ambulatory blood pressure monitoring. On reviewing the notes it appears her blood pressure four weeks ago was 146/88 mmHg. A urine dipstick shows protein + and nothing else. There is no significant past medical history of note. What is the most likely diagnosis?

- ☐ A. Pre-eclampsia
- ☐ B. Pregnancy-induced hypertension
- ☐ C. White-coat hypertension
- ☐ D. Normal physiological change
- ☐ E. Pre-existing hypertension

This lady has pre-existing hypertension. Pregnancy related blood pressure problems (such as pregnancy-induced hypertension or pre-eclampsia) do not occur before 20 weeks. The raised ambulatory blood pressure readings exclude a diagnosis of white-coat hypertension.

Note the use of the term 'pre-existing hypertension' rather than essential hypertension. Raised blood pressure in a 36-year-old female is not that common and raises the possibility of secondary hypertension.

### Hypertension in pregnancy

The classification of hypertension in pregnancy is complicated and varies. Remember, in normal pregnancy:

- blood pressure usually falls in the first trimester (particularly the diastolic), and continues to fall until 20-24 weeks
- after this time the blood pressure usually increases to pre-pregnancy levels by term

Hypertension in pregnancy is usually defined as:

- systolic > 140 mmHg or diastolic > 90 mmHg
- or an increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic

After establishing that the patient is hypertensive they should be categorised into one of the following groups

Pre-existing hypertension	Pregnancy-induced hypertension (PIH, also known as gestational hypertension)	Pre-eclampsia
A history of hypertension before pregnancy or an elevated blood pressure > 140/90 mmHg before 20 weeks gestation	Hypertension (as defined above) occurring in the second half of pregnancy (i.e. after 20 weeks)	Pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours)
No proteinuria, no oedema	No proteinuria, no oedema	Oedema may occur but is now less commonly used as a criteria
Occurs in 3-5% of pregnancies and is more common in older women	Occurs in around 5-7% of pregnancies	Occurs in around 5% of pregnancies
	Resolves following birth (typically after one month). Women with PIH are at increased risk of future pre-eclampsia or hypertension later in life	



**Question 33 of 247**

Next

A 52-year-old female with a known history of systemic sclerosis presents for annual review to the rheumatology clinic. Which one of the following symptoms is most characteristic in patients who have developed pulmonary arterial hypertension?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Exertional dyspnoea           |
| <input type="radio"/> | B. Paroxysmal nocturnal dyspnoea |
| <input type="radio"/> | C. Cough                         |
| <input type="radio"/> | D. Early morning dyspnoea        |
| <input type="radio"/> | E. Orthopnoea                    |

**Pulmonary arterial hypertension: features and management**

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise.

**Features**

- exertional dyspnoea is the most frequent symptom
- chest pain and syncope may also occur
- loud P2
- left parasternal heave (due to right ventricular hypertrophy)

Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy. Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide

If there is a positive response to acute vasodilator testing

- oral calcium channel blockers

If there is a negative response to acute vasodilator testing

- prostacyclin analogues: treprostinil, iloprost
- endothelin receptor antagonists: bosentan
- phosphodiesterase inhibitors: sildenafil

Which one of the following features would indicate cardiac tamponade rather than constrictive pericarditis?

- ☐ A. Raised JVP
- ☐ B. Muffled heart sounds
- ☐ C. No Y descent on JVP
- ☐ D. Hypotension
- ☐ E. Tachycardia

[Next question](#)

In cardiac tamponade there is characteristically no Y descent on the JVP. The other four features are seen in both cardiac tamponade and constrictive pericarditis

### Cardiac tamponade

#### Features

- dyspnoea
- raised JVP, with an absent Y descent - this is due to the limited right ventricular filling
- tachycardia
- hypotension
- muffled heart sounds
- pulsus paradoxus
- Kussmaul's sign (much debate about this)
- ECG: electrical alternans

The key differences between constrictive pericarditis and cardiac tamponade are summarised in the table below:

	Cardiac tamponade	Constrictive pericarditis
<b>JVP</b>	Absent Y descent	X + Y present
<b>Pulsus paradoxus</b>	Present	Absent
<b>Kussmaul's sign</b>	Rare	Present
<b>Characteristic features</b>		Pericardial calcification on CXR

A commonly used mnemonic to remember the absent Y descent in cardiac tamponade is TAMponade = TAMpaX

A 24-year-old male is diagnosed as having hypertrophic obstructive cardiomyopathy. Which one of the following markers is most useful in assessing risk of sudden death?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Abnormal blood pressure changes on exercise |
| <input type="radio"/> | B. Left ventricular outflow tract gradient     |
| <input type="radio"/> | C. QT interval                                 |
| <input type="radio"/> | D. Right atrial diameter                       |
| <input type="radio"/> | E. QRS duration                                |

[Next question](#)

### HOCM: prognostic factors

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. Mutations to various proteins including beta-myosin, alpha-tropomyosin and troponin T have been identified. Septal hypertrophy causes left ventricular outflow obstruction. It is an important cause of sudden death in apparently healthy individuals.

Poor prognostic factors

- syncope
- family history of sudden death
- young age at presentation
- non-sustained ventricular tachycardia on 24 or 48-hour Holter monitoring
- abnormal blood pressure changes on exercise

An increased septal wall thickness is also associated with a poor prognosis.

Each one of the following is associated with right axis deviation on ECG, except:

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Right ventricular hypertrophy                                    |
| <input type="radio"/> | B. Pulmonary embolism   |
| <input type="radio"/> | C. Wolf-Parkinson-White syndrome with right-sided accessory pathway |
| <input type="radio"/> | D. Chronic lung disease   |
| <input type="radio"/> | E. Left posterior hemiblock   |

Next question

Wolff-Parkinson-White syndrome is associated with a short PR interval and a wide QRS complex with a slurred upstroke, termed a delta wave. Axis deviation depends on the position of the accessory pathway

### ECG: axis deviation

Causes of left axis deviation (LAD)

- left anterior hemiblock
- left bundle branch block
- Wolff-Parkinson-White syndrome\* - right-sided accessory pathway
- hyperkalaemia
- congenital: ostium primum ASD, tricuspid atresia
- minor LAD in obese people

Causes of right axis deviation (RAD)

- right ventricular hypertrophy
- left posterior hemiblock
- chronic lung disease
- pulmonary embolism
- ostium secundum ASD
- Wolff-Parkinson-White syndrome\* - left-sided accessory pathway
- normal in infant < 1 years old
- minor RAD in tall people

\*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

A 28-year-old intravenous drug user is brought into the Emergency Department as a stand-by call following a cardiac arrest. He has been using methadone for the past 3 months. Unfortunately attempts to resuscitate him fail. Which one of following underlying problems is most likely to have caused his sudden death?

- ☐ A. Prolonged QT interval
- ☐ B. Complete heart block
- ☐ C. Pulmonary arterial hypertension
- ☐ D. Cardiomyopathy
- ☐ E. Hypokalaemia

Next question

Methadone is a common cause of QT prolongation

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"> <li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li> <li>Romano-Ward syndrome (no deafness)</li> </ul>	<ul style="list-style-type: none"> <li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li> <li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li> <li>methadone</li> <li>chloroquine</li> <li>terfenadine**</li> <li>erythromycin</li> </ul>	<ul style="list-style-type: none"> <li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li> <li>acute myocardial infarction</li> <li>myocarditis</li> <li>hypothermia</li> <li>subarachnoid haemorrhage</li> </ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming

- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

## Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

A 60-year-old man is transferred from the local psychiatric unit to the Emergency Department. Throughout the day he has complained of palpitations and feeling light-headed. The psychiatry consultant noted he was tachycardic and requested a transfer. An ECG taken following admission shows a broad complex tachycardia consistent with torsades de pointes, rate 120/min. His blood pressure is 122/80 mmHg and there are no signs of heart failure. What is the most appropriate management?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Intravenous naloxone           |
| <input type="radio"/> | B. Intravenous magnesium sulphate |
| <input type="radio"/> | C. DC cardioversion               |
| <input type="radio"/> | D. Intravenous amiodarone         |
| <input type="radio"/> | E. Intravenous verapamil          |

[Next question](#)

### Torsades de pointes

Torsades de pointes ('twisting of the points') is a rare arrhythmia associated with a long QT interval. It may deteriorate into ventricular fibrillation and hence lead to sudden death

#### Causes of long QT interval

- congenital: Jervell-Lange-Nielsen syndrome, Romano-Ward syndrome
- antiarrhythmics: amiodarone, sotalol, class 1a antiarrhythmic drugs
- tricyclic antidepressants
- antipsychotics
- chloroquine
- terfenadine
- erythromycin
- electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia
- myocarditis
- hypothermia
- subarachnoid haemorrhage

#### Management

- IV magnesium sulphate

A 50-year-old man is admitted to Resus with a suspected anterior myocardial infarction. An ECG on arrival confirms the diagnosis and thrombolysis is prepared. The patient is stable and his pain is well controlled with intravenous morphine. Clinical examination shows a blood pressure of 140/84 mmHg, pulse 90 bpm and oxygen saturations on room air of 97%. What is the most appropriate management with regards to oxygen therapy?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. 2-4 l/min via nasal cannulae |
| <input type="radio"/> | B. No oxygen therapy            |
| <input type="radio"/> | C. 15 l/min via reservoir mask  |
| <input type="radio"/> | D. 28% via Venturi mask         |
| <input type="radio"/> | E. 35% via Venturi mask         |

[Next question](#)

Please see the note below and provided link - there are now specific guidelines relating to the use of oxygen in emergency situations.

### Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive

- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

**Antithrombin** treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patient's creatinine is  $> 265 \mu\text{mol/l}$  unfractionated heparin should be given.

**Clopidogrel** 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.



**Coronary angiography** should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

<b>Aspirin</b>	Antiplatelet - inhibits the production of thromboxane A <sub>2</sub>
<b>Clopidogrel</b>	Antiplatelet - inhibits ADP binding to its platelet receptor
<b>Enoxaparin</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Fondaparinux</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Bivalirudin</b>	Reversible direct thrombin inhibitor

### Question 40 of 247

A 60-year-old man is admitted with palpitations to the Emergency Department. An ECG on admission shows a broad complex tachycardia at a rate of 150 bpm. His blood pressure is 124/82 mmHg and there is no evidence of heart failure. Which one of the following is it least appropriate to give?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Procainamide          |
| <input type="radio"/> | B. Lidocaine             |
| <input type="radio"/> | C. Synchronised DC shock |
| <input type="radio"/> | D. Adenosine             |
| <input type="radio"/> | E. Verapamil             |

[Next question](#)

Ventricular tachycardia - verapamil is contraindicated

Verapamil should never be given to a patient with a broad complex tachycardia as it may precipitate ventricular fibrillation in patients with ventricular tachycardia. Adenosine is sometimes given in this situation as a 'trial' if there is a strong suspicion the underlying rhythm is a supraventricular tachycardia with aberrant conduction

#### Ventricular tachycardia: management

Whilst a broad complex tachycardia may result from a supraventricular rhythm with aberrant conduction, the European Resuscitation Council advise that in a peri-arrest situation it is assumed to be ventricular in origin

If the patient has adverse signs (systolic BP < 90 mmHg, chest pain, heart failure or rate > 150 beats/min) then immediate cardioversion is indicated. In the absence of such signs antiarrhythmics may be used. If these fail, then electrical cardioversion may be needed with synchronised DC shocks

#### Drug therapy

- amiodarone: ideally administered through a central line
- lidocaine: use with caution in severe left ventricular impairment
- procainamide

Verapamil should NOT be used in VT

#### If drug therapy fails

- electrophysiological study (EPS)
- implantable cardioverter-defibrillator (ICD) - this is particularly indicated in patients with significantly impaired LV function

A 41-year-old man is admitted with left-sided pleuritic chest pain. He has a dry cough and reports that the pain is relieved by sitting forward. For the past three days he has been experiencing flu-like symptoms. Given the likely diagnosis, what is the most likely finding on ECG?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Large S wave in lead I, a large Q wave in lead III and an inverted T wave in lead III |
| <input type="radio"/> | B. Atrial fibrillation   |
| <input type="radio"/> | C. Widespread ST elevation   |
| <input type="radio"/> | D. ST segment depression in the anterior leads   |
| <input type="radio"/> | E. Hyperacute T waves  |

[Next question](#)

## Pericarditis

Pericarditis is one of the differentials of any patient presenting with chest pain.

### Features

- chest pain: may be pleuritic. Is often relieved by sitting forwards
- other symptoms include non-productive cough, dyspnoea and flu-like symptoms
- pericardial rub
- tachypnoea
- tachycardia

### Causes

- viral infections (Coxsackie)
- tuberculosis
- uraemia (causes 'fibrinous' pericarditis)
- trauma
- post-myocardial infarction, Dressler's syndrome
- connective tissue disease
- hypothyroidism

### ECG changes

- widespread 'saddle-shaped' ST elevation
- PR depression

A 72-year-old man is investigated for exertional chest pain and has a positive exercise tolerance test. He declines an angiogram and is discharged on a combination of aspirin 75mg od, simvastatin 40mg on, atenolol 50mg od and a GTN spray prn. Examination reveals a pulse of 72 bpm and a blood pressure of 130/80 mmHg. On review he is still regularly using his GTN spray. What is the most appropriate next step in management?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. Add nifedipine MR 30mg od          |
| <input type="radio"/> | B. Add isosorbide mononitrate 30mg bd |
| <input type="radio"/> | C. Increase atenolol to 100mg od      |
| <input type="radio"/> | D. Add nicorandil 10mg bd             |
| <input type="radio"/> | E. Add verapamil 80mg tds             |

[Next question](#)

The BNF recommends an atenolol dose of 100mg daily in 1 or 2 doses for angina. The starting dose of isosorbide mononitrate is 10mg bd.

### Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery. NICE produced guidelines in 2011 covering the management of stable angina

#### Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- NICE recommend using either a beta-blocker or a calcium channel blocker first-line based on 'comorbidities, contraindications and the person's preference'
- if a calcium channel blocker is used as monotherapy a rate-limiting one such as verapamil or diltiazem should be used. If used in combination with a beta-blocker then use a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine). Remember that beta-blockers should not be prescribed concurrently with verapamil (risk of complete heart block)
- if there is a poor response to initial treatment then medication should be increased to the maximum tolerated dose (e.g. for atenolol 100mg od)
- if a patient is still symptomatic after monotherapy with a beta-blocker add a calcium channel blocker and vice versa
- if a patient is on monotherapy and cannot tolerate the addition of a calcium channel blocker or a beta-blocker then consider one of the following drugs: a long-acting nitrate, ivabradine, nicorandil or ranolazine
- if a patient is taking both a beta-blocker and a calcium-channel blocker then only add a third drug whilst a patient is awaiting assessment for PCI or CABG

#### Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy
- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

#### Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the  $I_f$  ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

### Question 43 of 247

Which one of the following conditions is most associated with a bisferiens pulse?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Cardiac tamponade               |
| <input type="radio"/> | B. Severe left ventricular failure |
| <input type="radio"/> | C. Aortic stenosis                 |
| <input type="radio"/> | D. Patent ductus arteriosus        |
| <input type="radio"/> | E. Mixed aortic valve disease      |

[Next question](#)

## Pulses

### Pulsus paradoxus

- greater than the normal (10 mmHg) fall in systolic blood pressure during inspiration --> faint or absent pulse in inspiration
- severe asthma, cardiac tamponade

### Slow-rising/plateau

- aortic stenosis

### Collapsing

- aortic regurgitation
- patent ductus arteriosus
- hyperkinetic (anaemia, thyrotoxic, fever, exercise/pregnancy)

### Pulsus alternans

- regular alternation of the force of the arterial pulse
- severe LVF

### Bisferiens pulse

- 'double pulse' - two systolic peaks
- mixed aortic valve disease

'Jerky' pulse

- hypertrophic obstructive cardiomyopathy\*

\*HOCM may occasionally be associated with a bisferiens pulse

Next

### Question 44 of 247

What is the most common cardiac defect seen in patients with Down's syndrome?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Ventricular septal defect     |
| <input type="radio"/> | B. Endocardial cushion defect    |
| <input type="radio"/> | C. Secundum atrial septal defect |
| <input type="radio"/> | D. Tetralogy of Fallot           |
| <input type="radio"/> | E. Patent ductus arteriosus      |

Endocardial cushion defects account for about 40% of congenital heart disease seen in patients with Down's syndrome

### Down syndrome: features

#### Clinical features

- face: upslanting palpebral fissures, epicanthic folds, Brushfield spots in iris, protruding tongue, small ears, round/flat face
- flat occiput
- single palmar crease, pronounced 'sandal gap' between big and first toe
- hypotonia
- congenital heart defects (40-50%, see below)
- duodenal atresia
- Hirschsprung's disease

#### Cardiac complications

- multiple cardiac problems may be present
- endocardial cushion defect (c. 40%, also known as atrioventricular septal canal defects)
- ventricular septal defect (c. 30%)
- secundum atrial septal defect (c. 10%)
- tetralogy of Fallot (c. 5%)
- isolated patent ductus arteriosus (c. 5%)

#### Later complications

- subfertility: males are almost always infertile due to impaired spermatogenesis. Females are usually subfertile, and have an increased incidence of problems with pregnancy and labour
- learning difficulties
- short stature
- repeated respiratory infections (+hearing impairment from glue ear)
- acute lymphoblastic leukaemia
- hypothyroidism
- Alzheimer's
- atlantoaxial instability



A 17-year-old male is taken to the Emergency Department due to alcohol intoxication. On examination he is noted to be tachycardic with a rate of 140bpm. An ECG shows atrial fibrillation. The following morning he is noted to be in sinus rhythm. What is the most appropriate management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Sotalol and aspirin                  |
| <input type="radio"/> | B. Sotalol and warfarin                 |
| <input type="radio"/> | C. Refer for accessory pathway ablation |
| <input type="radio"/> | D. Amiodarone and aspirin               |
| <input type="radio"/> | E. Discharge                            |

[Next question](#)

Supraventricular arrhythmias secondary to acute alcohol intake are well characterised and have been termed 'holiday heart syndrome'. No specific treatment is required

### Atrial fibrillation: classification

An attempt was made in the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines to simplify and clarify the classification of atrial fibrillation (AF).

It is recommended that AF be classified into 3 patterns:

- first detected episode (irrespective of whether it is symptomatic or self-terminating)
- recurrent episodes, when a patient has 2 or more episodes of AF. If episodes of AF terminate spontaneously then the term **paroxysmal AF** is used. Such episodes last less than 7 days (typically < 24 hours). If the arrhythmia is not self-terminating then the term **persistent AF** is used. Such episodes usually last greater than 7 days
- in **permanent AF** there is continuous atrial fibrillation which cannot be cardioverted or if attempts to do so are deemed inappropriate. Treatment goals are therefore rate control and anticoagulation if appropriate

A woman who is 34 weeks pregnant is admitted to the obstetric ward. She has been monitored for the past few weeks due to pregnancy-induced hypertension but has now developed proteinuria. Her blood pressure is 162/94 mmHg. Which one of the following antihypertensives is it most appropriate to commence?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Nifedipine |
| <input type="radio"/> | B. Atenolol   |
| <input type="radio"/> | C. Labetalol  |
| <input type="radio"/> | D. Losartan   |
| <input type="radio"/> | E. Methyldopa |

[Next question](#)

Labetalol is first-line for pregnancy-induced hypertension

## Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria ( $> 0.3\text{g} / 24 \text{ hours}$ ). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

### Risk factors

- $> 40$  years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index  $> 30 \text{ kg/m}^2$
- diabetes mellitus
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

## Features of severe pre-eclampsia

- hypertension: typically > 170/110 mmHg and proteinuria as above
- proteinuria: dipstick ++/+++
- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count <  $100 \times 10^6/l$ , abnormal liver enzymes or HELLP syndrome

## Management

- consensus guidelines recommend treating blood pressure > 160/110 mmHg although many clinicians have a lower threshold
- oral labetalol is now first-line following the 2010 NICE guidelines. Nifedipine and hydralazine may also be used
- delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario

Next

### Question 47 of 247

Which one of the following drugs causes shortening of the QT interval?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Digoxin                   |
| <input type="radio"/> | B. Sotalol                   |
| <input type="radio"/> | C. Amiodarone                |
| <input type="radio"/> | D. Tricyclic antidepressants |
| <input type="radio"/> | E. Chloroquine               |

[Next question](#)

Digoxin causes shortening of the QT interval whilst the other four drugs cause QT prolongation

### Digoxin and digoxin toxicity

Digoxin is a cardiac glycoside now mainly used for rate control in the management of atrial fibrillation. As it has positive inotropic properties it is sometimes used for improving symptoms (but not mortality) in patients with heart failure.

Mechanism of action

- decreases conduction through the atrioventricular node which slows the ventricular rate in atrial fibrillation and flutter
- increases the force of cardiac muscle contraction due to inhibition of the  $\text{Na}^+/\text{K}^+$ ATPase pump

### Digoxin toxicity

Plasma concentration alone does not determine whether a patient has developed digoxin toxicity. The BNF advises that the likelihood of toxicity increases progressively from 1.5 to 3 mcg/l.

Features

- generally unwell, lethargy, nausea & vomiting, anorexia, confusion, yellow-green vision
- arrhythmias (e.g. AV block, bradycardia)

Precipitating factors

- classically: hypokalaemia\*
- increasing age
- renal failure
- myocardial ischaemia
- hypomagnesaemia, hypercalcaemia, hypernatraemia, acidosis
- hypoalbuminaemia

- hypothermia
- hypothyroidism
- drugs: amiodarone, quinidine, verapamil, diltiazem, spironolactone (compete for secretion in distal convoluted tubule therefore reduce excretion). Also drugs which cause hypokalaemia e.g. thiazides and loop diuretics

## Management

- Digibind
- correct arrhythmias
- monitor potassium

\*hyperkalaemia may also worsen digoxin toxicity, although this is very small print

### Question 48 of 247

A 45-year-old man is diagnosed with endocarditis of the aortic valve. He is treated with intravenous benzylpenicillin and gentamicin. What is the most important ECG change to monitor for?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Left ventricular hypertrophy (by voltage criteria) |
| <input type="radio"/> | B. Reflex tachycardia                                 |
| <input type="radio"/> | C. ST segment depression                              |
| <input type="radio"/> | D. Prolonged QT interval                              |
| <input type="radio"/> | E. Prolonged PR interval                              |

[Next question](#)

A prolonged PR interval could indicate the development of an aortic abscess, an indication for surgery

#### ECG: PR interval

Causes of a prolonged PR interval

- idiopathic
- ischaemic heart disease
- digoxin toxicity
- hypokalaemia\*
- rheumatic fever
- aortic root pathology e.g. abscess secondary to endocarditis
- Lyme disease
- sarcoidosis
- myotonic dystrophy

A prolonged PR interval may also be seen in athletes

\*hyperkalaemia can rarely cause a prolonged PR interval, but this is a much less common association than hypokalaemia

A 25-year-old woman is brought to the Emergency Department by a friend. She developed palpitations around 30 minutes ago whilst drinking a cup of coffee. Her only past medical history of note is asthma and menorrhagia for which she uses a salbutamol inhaler and takes tranexamic acid respectively. The admission ECG shows a supraventricular tachycardia at a rate of 160 bpm. Vagal manoeuvres are unsuccessful. What is the most appropriate next step in her management?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Intravenous verapamil    |
| <input type="radio"/> | B. Intravenous amiodarone   |
| <input type="radio"/> | C. Intravenous adenosine    |
| <input type="radio"/> | D. Electrical cardioversion |
| <input type="radio"/> | E. Intravenous esmolol      |

[Next question](#)

The administration of adenosine is contraindicated by her history of asthma. Verapamil should therefore be given.

### Supraventricular tachycardia

Whilst strictly speaking the term supraventricular tachycardia (SVT) refers to any tachycardia that is not ventricular in origin the term is generally used in the context of paroxysmal SVT. Episodes are characterised by the sudden onset of a narrow complex tachycardia, typically an atrioventricular nodal re-entry tachycardia (AVNRT). Other causes include atrioventricular re-entry tachycardias (AVRT) and junctional tachycardias.

#### Acute management

- vagal manoeuvres: e.g. Valsalva manoeuvre
- intravenous adenosine: contraindicated in asthmatics - verapamil is a preferable option
- electrical cardioversion

#### Prevention of episodes

- beta-blockers
- radio-frequency ablation

A 37-year-old woman who was investigated for progressive shortness-of-breath is diagnosed with primary pulmonary hypertension and started on bosentan. What is the mechanism of action of bosentan?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Activator of soluble guanylate cyclase |
| <input type="radio"/> | B. Phosphodiesterase type 5 inhibitors    |
| <input type="radio"/> | C. Endothelin receptor antagonist         |
| <input type="radio"/> | D. Prostanoid                             |
| <input type="radio"/> | E. Slow calcium channel blocker           |

[Next question](#)

Bosentan - endothelin-1 receptor antagonist

### Primary pulmonary hypertension

The classification of pulmonary hypertension is currently changing with the term idiopathic pulmonary arterial hypertension (IPAH) becoming more widely used

Primary pulmonary hypertension (PPH, now IPAH)

- pulmonary arterial pressure > 25 mmHg at rest, > 30mmHg with exercise
- PPH is diagnosed when no underlying cause can be found
- around 10% of cases are familial: autosomal dominant
- endothelin thought to play a key role in pathogenesis
- associated with HIV, cocaine and anorexigens (e.g. fenfluramine)

Features

- more common in females, typically presents at 20-40 years old
- progressive SOB
- cyanosis
- right ventricular heave, loud P2, raised JVP with prominent 'a' waves, tricuspid regurgitation

Investigation

- echocardiography



## Management

- diuretics if right heart failure
- anticoagulation
- vasodilator therapy: calcium channel blocker, IV prostaglandins, bosentan: endothelin-1 receptor antagonist
- heart-lung transplant

Next

### Question 51 of 247

Which part of the jugular venous waveform is associated with the closure of the tricuspid valve?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. a wave        |
| <input type="radio"/> | <b>B. c wave</b> |
| <input type="radio"/> | C. x descent     |
| <input type="radio"/> | D. y descent     |
| <input type="radio"/> | E. v wave        |

[Next question](#)

JVP: C wave - closure of the tricuspid valve

The c wave of the jugular venous waveform is associated with the closure of the tricuspid valve

#### Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis.

'a' wave = atrial contraction

- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves

- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave

- closure of tricuspid valve
- not normally visible

'v' wave

- due to passive filling of blood into the atrium against a closed tricuspid valve

- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve

Next

### Question 52 of 247

A 71-year-old woman presents with palpitations and 'lightheadedness'. An ECG shows that she is in atrial fibrillation with a rate of 130 / min. Her blood pressure is normal and examination of her cardiorespiratory system is otherwise unremarkable. Her past medical history includes well controlled asthma (salbutamol & beclomethasone) and depression (citalopram). Her symptoms have been present for around three days. What is the most appropriate medication to use for rate control?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Diltiazem  |
| <input type="radio"/> | B. Sotalol    |
| <input type="radio"/> | C. Digoxin    |
| <input type="radio"/> | D. Atenolol   |
| <input type="radio"/> | E. Amiodarone |

[Next question](#)

Her history of asthma is a contraindication to the prescription of a beta-blocker. NICE therefore recommend a rate-limiting calcium channel blocker.

Consideration should also be given to antithrombotic therapy.

#### Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
Older than 65 years History of ischaemic heart disease	Younger than 65 years Symptomatic First presentation Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) Congestive heart failure

Next

### Question 53 of 247

A 62-year-old man is referred from the Emergency Department with a pulse of 40 beats/min. Which one of the following factors carries the least risk of asystole when risk stratifying the patient?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Ventricular pause of 5 seconds                 |
| <input type="radio"/> | B. Recent asystole                                |
| <input type="radio"/> | C. Complete heart block with a narrow complex QRS |
| <input type="radio"/> | D. Mobitz type II AV block                        |
| <input type="radio"/> | E. Complete heart block with a broad complex QRS  |

[Next question](#)

Complete heart block with a narrow complex QRS complex carries the least risk of asystole as the atrioventricular junctional pacemaker may provide an haemodynamically acceptable and stable heart rate. The other four factors are indications for transvenous pacing

### Peri-arrest rhythms: bradycardia

The 2010 Resuscitation Council (UK) guidelines emphasise that the management of bradycardia depends on:

- 1. identifying the presence of signs indicating haemodynamic compromise - 'adverse signs'
- 2. identifying the potential risk of asystole

### Adverse signs

The following factors indicate haemodynamic compromise and hence the need for treatment:

- shock: hypotension (systolic blood pressure < 90 mmHg), pallor, sweating,

cold, clammy extremities, confusion or impaired consciousness

- syncope
- myocardial ischaemia
- heart failure

Atropine is the first line treatment in this situation. If this fails to work, or there is the potential risk of asystole then transvenous pacing is indicated

### Potential risk of asystole

The following indicate a potential risk of asystole and hence the need for treatment with transvenous pacing:

- complete heart block with broad complex QRS

- recent asystole
- Mobitz type II AV block
- ventricular pause > 3 seconds

If there is a delay in the provision of transvenous pacing the following interventions may be used:

- atropine, up to maximum of 3mg
- transcutaneous pacing
- adrenaline infusion titrated to response

Next

### Question 54 of 247

A 34-year-old man is seen in the cardiology clinic. He has been referred by his GP with a history of increasing dyspnoea and exercise-related syncope. His father died suddenly when at the age of 42-years-old. An ECG attached to the admission letter shows left ventricular hypertrophy with widespread T wave inversion. Given the likely diagnosis, what is the most appropriate next investigation?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Cardiac angiogram     |
| <input type="radio"/> | B. Transthoracic echo    |
| <input type="radio"/> | C. Transoesophageal echo |
| <input type="radio"/> | D. Exercise ECG          |
| <input type="radio"/> | E. 24-hour ECG           |

The likely diagnosis is hypertrophic obstructive cardiomyopathy which should be investigated with a transthoracic echocardiogram

### HOCM: features

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

#### Features

- often asymptomatic
- dyspnoea, angina, syncope
- sudden death (most commonly due to ventricular arrhythmias), arrhythmias, heart failure
- jerky pulse, large 'a' waves, double apex beat
- ejection systolic murmur: increases with Valsalva manoeuvre and decreases on squatting

#### Associations

- Friedreich's ataxia
- Wolff-Parkinson White

#### Echo - mnemonic - MR SAM ASH

- mitral regurgitation (MR)
- systolic anterior motion (SAM) of the anterior mitral valve leaflet
- asymmetric hypertrophy (ASH)

#### ECG



- left ventricular hypertrophy
- progressive T wave inversion
- deep Q waves
- atrial fibrillation may occasionally be seen

Next

### Question 55 of 247

Which one of the following features is not part of the modified Duke criteria used in the diagnosis of infective endocarditis?

<input type="radio"/>	A. Fever > 38°C
<input type="radio"/>	B. Positive molecular assays for specific gene targets
<input type="radio"/>	C. Indwelling central line
<input type="radio"/>	D. Intravenous drug use
<input type="radio"/>	E. Janeway lesions

Next question

The modified Duke criteria have now been adopted in the latest guidelines from the European Society of Cardiology. Details can be found in the link below

#### Infective endocarditis: Modified Duke criteria

Infective endocarditis diagnosed if

- pathological criteria positive, or
- 2 major criteria, or
- 1 major and 3 minor criteria, or
- 5 minor criteria

#### Pathological criteria

Positive histology or microbiology of pathological material obtained at autopsy or cardiac surgery (valve tissue, vegetations, embolic fragments or intracardiac abscess content)

#### Major criteria

Positive blood cultures

- two positive blood cultures showing typical organisms consistent with infective endocarditis, such as *Streptococcus viridans* and the HACEK group, or
- persistent bacteraemia from two blood cultures taken > 12 hours apart or three or more positive blood cultures where the pathogen is less specific such as *Staph aureus* and *Staph epidermidis*, or
- positive serology for *Coxiella burnetii*, *Bartonella* species or *Chlamydia psittaci*, or
- positive molecular assays for specific gene targets

Evidence of endocardial involvement

- positive echocardiogram (oscillating structures, abscess formation, new valvular regurgitation or dehiscence of prosthetic valves), or
- new valvular regurgitation

#### **Minor criteria**

- predisposing heart condition or intravenous drug use
- microbiological evidence does not meet major criteria
- fever  $> 38^{\circ}\text{C}$
- vascular phenomena: major emboli, splenomegaly, clubbing, splinter haemorrhages, petechiae or purpura
- immunological phenomena: glomerulonephritis, Osler's nodes, Roth spots, Janeway lesions

Next

### Question 56 of 247

A 57-year-old man presents to the Emergency Department with palpitations for the past 36 hours. He has no past history of note. There is no associated chest pain or shortness of breath. Clinical examination is unremarkable other than an irregular tachycardia. An ECG shows atrial fibrillation at a rate of 126 bpm with no other changes. What is the most appropriate management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Beta-blocker + warfarin  |
| <input type="radio"/> | B. Digoxin + aspirin  |
| <input type="radio"/> | C. Heparinise + cardioversion in the Emergency Department                             |
| <input type="radio"/> | D. Beta-blocker + aspirin   |
| <input type="radio"/> | E. Warfarinise + transthoracic echo with elective electrical cardioversion in 4 weeks |

[Next question](#)

This patient is a good example of someone who would benefit from electrical cardioversion.

#### Atrial fibrillation: cardioversion

##### Onset < 48 hours

If the atrial fibrillation (AF) is definitely of less than 48 hours onset patients should be heparinised. Patients who have risk factors for ischaemic stroke should be put on lifelong oral anticoagulation. Otherwise, patients may be cardioverted using either:

- electrical - 'DC cardioversion'
- pharmacology - amiodarone if structural heart disease, flecainide in those without structural heart disease

Following electrical cardioversion if AF is confirmed as being less than 48 hours duration then further anticoagulation is unnecessary

##### Onset > 48 hours

If the patient has been in AF for more than 48 hours then anticoagulation should be given for at least 3 weeks prior to cardioversion. An alternative strategy is to perform a transoesophageal echo (TOE) to exclude a left atrial appendage (LAA) thrombus. If excluded patients may be heparinised and cardioverted immediately.

If there is a high risk of cardioversion failure (e.g. Previous failure or AF recurrence) then it is recommend to have at least 4 weeks amiodarone or sotalol prior to electrical cardioversion

Following electrical cardioversion patients should be anticoagulated for at least 4 weeks. After this time decisions about anticoagulation should be taken on an individual basis depending on the risk of recurrence

A 35-year-old female presents with a deep vein thrombosis in the third trimester of pregnancy. Whilst in the Emergency Department she develops a left hemiparesis. What underlying cardiac abnormality is most likely to be responsible?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Primum ASD               |
| <input type="radio"/> | B. Secundum ASD             |
| <input type="radio"/> | C. Patent foramen ovale     |
| <input type="radio"/> | D. VSD                      |
| <input type="radio"/> | E. Patent ductus arteriosus |

[Next question](#)

Whilst atrial septal defects may allow emboli to pass from the right side of the heart to the left side, the most common cause is a patent foramen ovale

### Patent foramen ovale

Patent foramen ovale (PFO) is present in around 20% of the population. It may allow embolus (e.g. from DVT) to pass from right side of the heart to the left side leading to a stroke - 'a paradoxical embolus'

There also appears to be an association between migraine and PFO. Some studies have reported improvement in migraine symptoms following closure of the PFO

### Question 58 of 247

A 71-year-old patient presents to the Emergency Department with a two hour history of crushing central chest pain. He is known to have a history of ischaemic heart disease. The ECG shows the following:

- ST elevation greater in lead II than in lead III with abnormal Q waves in II, III, and aVF
- Tall R waves in V1-2, tall and pointed T waves in V1-V3
- ST elevation in V5-V6

Where is the lesion most likely to be?

<input type="radio"/>	A. Left anterior descending
<input type="radio"/>	B. Left circumflex
<input type="radio"/>	C. Right coronary artery
<input type="radio"/>	D. Left main stem
<input type="radio"/>	E. Posterior interventricular

[Next question](#)

These are classical findings of a circumflex occlusion. The table below shows how the changes correspond to the cardiac anatomy:

ST elevation greater in lead II than in lead III with abnormal Q waves in II, III, and aVF	Inferior infarction
Tall R waves in V1-2, tall and pointed T waves in V1V3	Posterior infarction
ST elevation in V5-V6	Lateral infarction

### ECG: coronary territories

The table below shows the correlation between ECG changes and coronary territories:

	ECG changes	Coronary artery
<b>Anteroseptal</b>	V1-V4	Left anterior descending
<b>Inferior</b>	II, III, aVF	Right coronary
<b>Anterolateral</b>	V4-6, I, aVL	Left anterior descending or left circumflex
<b>Lateral</b>	I, aVL +/- V5-6	Left circumflex
<b>Posterior</b>	Tall R waves V1-2	Usually left circumflex, also right coronary

**Question 59 of 247**

Next

A 72-year-old man is admitted to the Emergency Department with chest pain. On initial assessment he is noted to be pale, have a heart rate of 40/min and a blood pressure of 90/60 mmHg. Which one of the coronary arteries is most likely to be affected?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Posterior descending      |
| <input type="radio"/> | B. Left anterior descending  |
| <input type="radio"/> | C. Right coronary            |
| <input type="radio"/> | D. Anterior interventricular |
| <input type="radio"/> | E. Left circumflex           |

Next question

Complete heart block following a MI? - right coronary artery lesion

This patient has developed complete heart block secondary to a right coronary artery (RCA) infarction. The atrioventricular node is supplied by the posterior interventricular artery, which in the majority of patients is a branch of the right coronary artery. In the remainder of patients the posterior interventricular artery is supplied by the left circumflex artery.

**Complete heart block**

## Features

- syncope
- heart failure
- regular bradycardia (30-50 bpm)
- wide pulse pressure
- JVP: cannon waves in neck
- variable intensity of S1

A 1-year-old girl is noted to have a continuous murmur, loudest at the left sternal edge. She is not cyanosed. A diagnosis of patent ductus arteriosus is suspected. What pulse abnormality is most associated with this condition?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Collapsing pulse |
| <input type="radio"/> | B. Bisferiens pulse |
| <input type="radio"/> | C. Pulsus paradoxus |
| <input type="radio"/> | D. 'Jerky' pulse    |
| <input type="radio"/> | E. Pulsus alternans |

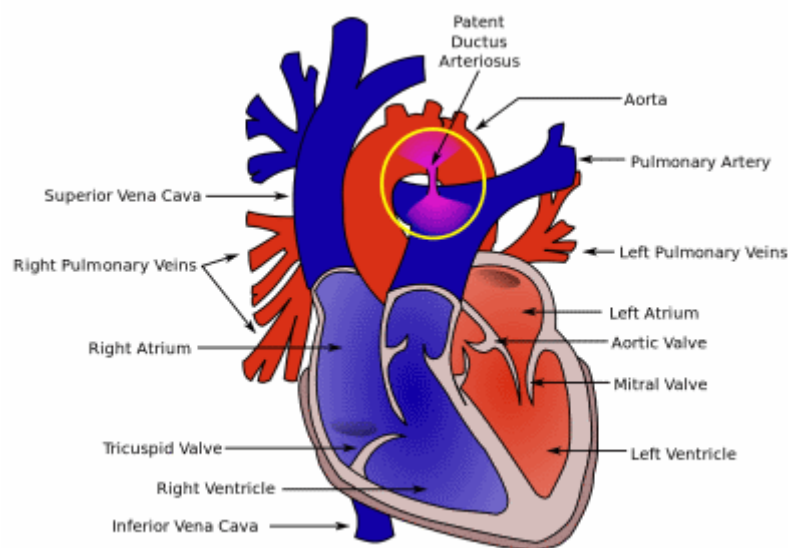
[Next question](#)

Patent ductus arteriosus - collapsing pulse

## Patent ductus arteriosus

### Overview

- acyanotic congenital heart defect
- connection between the pulmonary trunk and descending aorta
- more common in premature babies, born at high altitude or maternal rubella infection in the first trimester



### Features



- left subclavicular thrill
- continuous 'machinery' murmur
- large volume, bounding, collapsing pulse
- wide pulse pressure
- heaving apex beat

## Management

- indomethacin closes the connection in the majority of cases
- if associated with another congenital heart defect amenable to surgery then prostaglandin E1 is useful to keep the duct open until after surgical repair

Next

### Question 61 of 247

A 61-year-old woman is admitted to the Emergency Department with central chest pain. It feels like her previous angina but is not relieved by nitrates. She has a history of ischaemic heart disease and 4 weeks ago underwent a percutaneous coronary intervention during which a stent was placed. This is her first episode of angina since the procedure. What is the most likely diagnosis?

- ☐ A. Pericarditis
- ☐ B. Aortic dissection
- ☐ C. Coronary artery dissection
- ☐ D. Restenosis
- ☐ E. Stent thrombosis

[Next question](#)

### Percutaneous coronary intervention

Percutaneous coronary intervention (PCI) is a technique used to restore myocardial perfusion in patients with ischaemic heart disease, both in patients with stable angina and acute coronary syndromes. Stents are implanted in around 95% of patients - it is now rare for just balloon angioplasty to be performed

Following stent insertion migration and proliferation of smooth muscle cells and fibroblasts occur to the treated segment. The stent struts eventually become covered by endothelium. Until this happens there is an increased risk of platelet aggregation leading to thrombosis.

Two main complications may occur

- stent thrombosis: due to platelet aggregation as above. Occurs in 1-2% of patients, most commonly in the first month. Usually presents with acute myocardial infarction
- restenosis: due to excessive tissue proliferation around stent. Occurs in around 5-20% of patients, most commonly in the first 3-6 months. Usually presents with the recurrence of angina symptoms. Risk factors include diabetes, renal impairment and stents in venous bypass grafts

Types of stent

- bare-metal stent (BMS)
- drug-eluting stents (DES): stent coated with paclitaxel or rapamycin which inhibit local tissue growth. Whilst this reduces restenosis rates the stent thrombosis rates are increased as the process of stent endothelialisation is slowed

Following insertion the most important factor in preventing stent thrombosis is antiplatelet therapy. Aspirin should be continued indefinitely. The length of clopidogrel treatment depends on the type of stent, reason for insertion and consultant preference

Which of the following is responsible for the plateau phase of the myocardial action potential?

- ☐ A. Slow calcium efflux
- ☐ B. Efflux of potassium
- ☐ C. Rapid sodium influx
- ☐ D. Slow influx of calcium
- ☐ E. Slow sodium efflux

Next question

Slow influx of calcium is responsible for the plateau phase of the action potential

## Electrical activity of the heart

### Myocardial action potential

Phase	Description	Mechanism
0	Rapid depolarisation	Rapid sodium influx These channels automatically deactivate after a few ms
1	Early repolarisation	Efflux of potassium
2	Plateau	Slow influx of calcium
3	Final repolarisation	Efflux of potassium
4	Restoration of ionic concentrations	Resting potential is restored by $\text{Na}^+/\text{K}^+$ ATPase There is slow entry of $\text{Na}^+$ into the cell decreasing the potential difference until the threshold potential is reached, triggering a new action potential

NB cardiac muscle remains contracted 10-15 times longer than skeletal muscle

### Conduction velocity

Atrial conduction	Spreads along ordinary atrial myocardial fibres at 1 m/sec
AV node conduction	0.05 m/sec
Ventricular conduction	Purkinje fibres are of large diameter and achieve velocities of 2-4 m/sec (this allows a rapid and coordinated contraction of the ventricles)

A 40-year-old woman who is being treated for refractory hypertension undergoes a coronary angiogram after developing non-specific chest pains. The cardiologist takes a number of measurements during the procedure:

	Pressure (mmHg)
Right femoral artery	122/68
Left ventricle	202/104
Aorta	194/84

The blood pressure in her left arm taking during the procedure was 188/74 mmHg. What is the most likely underlying diagnosis?

- ☐ A. Left subclavian artery stenosis
- ☐ B. Renal artery stenosis
- ☐ C. Coarctation of the aorta
- ☐ D. Aortic stenosis
- ☐ E. Results consistent with essential hypertension

Next question

The most common type of coarctation of the aorta seen in adults is the postductal variety, i.e. the aortic narrowing is distal to the ductus arteriosus. This means that the upper limb blood pressure is greater than that in the lower limbs as the narrowing occurs after the left subclavian artery branches from the aorta.

Another approach to answering this question is to look at the history. A young person with refractory hypertension raises the possibility of secondary, rather than essential (primary) hypertension. The only two diagnoses listed above which cause hypertension are coarctation and renal artery stenosis. This narrows the diagnostic possibilities and makes the question easier to answer.

### Coarctation of the aorta

Coarctation of the aorta describes a congenital narrowing of the descending aorta.

#### Overview

- more common in males (despite association with Turner's syndrome)

#### Features

- infancy: heart failure
- adult: hypertension
- radio-femoral delay
- mid systolic murmur, maximal over back

- apical click from the aortic valve
- notching of the inferior border of the ribs (due to collateral vessels) is not seen in young children

#### Associations

- Turner's syndrome
- bicuspid aortic valve
- berry aneurysms
- neurofibromatosis

Next

### Question 64 of 247

A 57-year-old man who had a prosthetic mitral valve replacement 7 years ago presents with fever. An urgent echocardiogram shows features consistent with endocarditis. What is the most suitable antibiotic therapy until blood culture results are known?

- ☐ A. IV ceftriaxone + benzylpenicillin
- ☐ B. IV vancomycin + rifampicin + gentamicin
- ☐ C. IV benzylpenicillin + gentamicin
- ☐ D. IV flucloxacillin + gentamicin
- ☐ E. IV vancomycin + benzylpenicillin

[Next question](#)

If the patient has a prosthetic valve and endocarditis is suspected the initial therapy should consist of intravenous vancomycin + rifampicin + gentamicin.

### Infective endocarditis: prognosis and management

Poor prognostic factors

- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism

- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)

Scenario	Suggested antibiotic therapy
Initial blind therapy	Flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
Initial blind therapy if prosthetic valve is present or patient is penicillin allergic	Vancomycin + rifampicin + gentamicin
Endocarditis caused by staphylococci	Flucloxacillin (add rifampicin if prosthetic valve, vancomycin + rifampicin if penicillin allergic or MRSA)
Native valve endocarditis caused by fully-sensitive streptococci (e.g. viridans)	Benzylpenicillin (large vegetation, intracardial abscess or infected emboli then benzylpenicillin + gentamicin, vancomycin if penicillin allergic)

Native valve endocarditis caused by less sensitive streptococci  
OR prosthetic valve endocarditis caused by streptococci

Benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

#### Indications for surgery

- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

### Question 65 of 247

A 65-year-old female with a known history of heart failure presents for an annual check-up. She is found to have a blood pressure of 170/100 mmHg. Her current medications are furosemide and aspirin. What is the most appropriate medication to add?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Bendroflumethiazide |
| <input type="radio"/> | B. Spironolactone      |
| <input type="radio"/> | C. Bisoprolol          |
| <input type="radio"/> | D. Verapamil           |
| <input type="radio"/> | E. Enalapril           |

[Next question](#)

Both enalapril and bisoprolol have been shown to improve prognosis in patients with heart failure. Enalapril however would also be better at treating the hypertension. NICE guidelines recommend the introduction of an ACE inhibitor prior to a beta-blocker in patients with chronic heart failure

### Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:

- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:

- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin\* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off\*\* pneumococcal vaccine

\*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

\*\*adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years



A patient with severe aortic stenosis is noted to have a fourth heart sound. Which part of the ECG does this best correlate with?

- |                       |                |
|-----------------------|----------------|
| <input type="radio"/> | A. U wave      |
| <input type="radio"/> | B. QRS complex |
| <input type="radio"/> | C. P wave      |
| <input type="radio"/> | D. ST segment  |
| <input type="radio"/> | E. T wave      |

## Heart sounds

The first heart sound (S1) is caused by closure of the mitral and tricuspid valves whilst the second heart sound (S2) is due to aortic and pulmonary valve closure

### S1

- closure of mitral and tricuspid valves
- soft if long PR or mitral regurgitation
- loud in mitral stenosis

### S2

- closure of aortic and pulmonary valves
- soft in aortic stenosis
- splitting during inspiration is normal

### S3

- caused by diastolic filling of the ventricle
- considered normal if < 30 years old (may persist in women up to 50 years old)
- heard in left ventricular failure (e.g. dilated cardiomyopathy), constrictive pericarditis (called a pericardial knock)

### S4

- may be heard in aortic stenosis, HOCM, hypertension
- caused by atrial contraction against a stiff ventricle
- in HOCM a double apical impulse may be felt as a result of a palpable S4

Which of the following signs is not associated with the development of Eisenmenger's syndrome in a patient with a ventricular septal defect?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Worsening of systolic murmur               |
| <input type="radio"/> | B. Raised JVP                                 |
| <input type="radio"/> | C. Loud second heart sound                    |
| <input type="radio"/> | D. Cyanosis                                   |
| <input type="radio"/> | E. Large 'a' waves in jugular venous waveform |

[Next question](#)

Eisenmenger's syndrome is characterised by the reversal of the left-right shunt due to pulmonary hypertension. The original murmur may disappear once Eisenmenger's syndrome develops

### Eisenmenger's syndrome

Describes the reversal of a left to right shunt in a congenital heart defect due to pulmonary hypertension

Associated with

- VSD
- ASD
- PDA

Features

- original murmur may disappear
- cyanosis
- clubbing
- right ventricular failure
- haemoptysis, embolism

Management

- heart-lung transplantation is required

A 79-year-old woman is reviewed. She has taken bendroflumethiazide 2.5mg od for the past 10 years for hypertension. Her current blood pressure is 150/94 mmHg. Clinical examination is otherwise unremarkable. An echocardiogram from two months ago is reported as follows:

Ejection fraction 48%, moderate left ventricular hypertrophy. Minimal MR noted

What is the most appropriate next step in management?

- ☐ A. Increase bendroflumethiazide to 5mg od
- ☐ B. Stop bendroflumethiazide + start frusemide 40mg od
- ☐ C. Add ramipril 1.25mg od
- ☐ D. Stop bendroflumethiazide + start ramipril 1.25mg od
- ☐ E. Add amlodipine 5mg od

Next question

The echocardiogram shows a degree of left ventricular impairment. It is important an ACE inhibitor is started in such patients. This will help to both control her blood pressure and also slow the deterioration in her cardiac function.

A beta-blocker should also be added in the near future given the left ventricular impairment.

### Hypertension: diagnosis and management

NICE published updated guidelines for the management of hypertension in 2011. Some of the key changes include:

- classifying hypertension into stages
- recommending the use of ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM)
- calcium channel blockers are now considered superior to thiazides
- bendroflumethiazide is no longer the thiazide of choice

### Blood pressure classification

This becomes relevant later in some of the management decisions that NICE advocate.

<b>Stage 1 hypertension</b>	Clinic BP $\geq$ 140/90 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 135/85 mmHg
<b>Stage 2 hypertension</b>	Clinic BP $\geq$ 160/100 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 150/95 mmHg
<b>Severe hypertension</b>	Clinic systolic BP $\geq$ 180 mmHg, or clinic diastolic BP $\geq$ 110 mmHg

### Diagnosing hypertension

If a BP reading is  $\geq 140 / 90$  mmHg patients should be offered ABPM to confirm the diagnosis.

Patients with a BP reading of  $\geq 180/110$  mmHg should be considered for immediate treatment.

Ambulatory blood pressure monitoring (ABPM)

- at least 2 measurements per hour during the person's usual waking hours (for example, between 08:00 and 22:00)
- use the average value of at least 14 measurements

If ABPM is not tolerated or declined HBPM should be offered.

Home blood pressure monitoring (HBPM)

- for each BP recording, two consecutive measurements need to be taken, at least 1 minute apart and with the person seated
- BP should be recorded twice daily, ideally in the morning and evening
- BP should be recorded for at least 4 days, ideally for 7 days
- discard the measurements taken on the first day and use the average value of all the remaining measurements

## Managing hypertension

ABPM/HBPM  $\geq 135/85$  mmHg (i.e. stage 1 hypertension)

- treat if  $< 80$  years of age and any of the following apply; target organ damage, established cardiovascular disease, renal disease, diabetes or a 10-year cardiovascular risk equivalent to 20% or greater

ABPM/HBPM  $\geq 150/95$  mmHg (i.e. stage 2 hypertension)

- offer drug treatment regardless of age

For patients  $< 40$  years consider specialist referral to exclude secondary causes.

Step 1 treatment

- patients  $< 55$ -years-old: ACE inhibitor (A)
- patients  $> 55$ -years-old or of Afro-Caribbean origin: calcium channel blocker

Step 2 treatment

- ACE inhibitor + calcium channel blocker (A + C)

### Step 3 treatment

- add a thiazide diuretic (D, i.e. A + C + D)
- NICE now advocate using either chlorthalidone (12.5-25.0 mg once daily) or indapamide (1.5 mg modified-release once daily or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide

NICE define a clinic BP  $\geq 140/90$  mmHg after step 3 treatment with optimal or best tolerated doses as resistant hypertension. They suggest step 4 treatment or seeking expert advice

### Step 4 treatment

- consider further diuretic treatment
- if potassium  $< 4.5$  mmol/l add spironolactone 25mg od
- if potassium  $> 4.5$  mmol/l add higher-dose thiazide-like diuretic treatment
- if further diuretic therapy is not tolerated, or is contraindicated or ineffective, consider an alpha- or beta-blocker

If BP still not controlled seek specialist advice.

### Blood pressure targets

	Clinic BP	ABPM / HBPM
Age $< 80$ years	140/90 mmHg	135/85 mmHg
Age $> 80$ years	150/90 mmHg	145/85 mmHg

### New drugs

#### Direct renin inhibitors

- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

Which one of the following would not be considered a normal variant on the ECG of an athletic 28-year-old man?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Wenckebach phenomenon    |
| <input type="radio"/> | B. Sinus bradycardia        |
| <input type="radio"/> | C. Junctional rhythm        |
| <input type="radio"/> | D. First degree heart block |
| <input type="radio"/> | E. Left bundle branch block |

Next question

### ECG: normal variants

The following ECG changes are considered normal variants in an athlete:

- sinus bradycardia
- junctional rhythm
- first degree heart block
- Wenckebach phenomenon

Next

### Question 70 of 247

Which one of the following statements regarding B-type natriuretic peptide is incorrect?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Effective treatment for heart failure lowers a patients BNP level                  |
| <input type="radio"/> | B. Acts as a diuretic   |
| <input type="radio"/> | C. A hormone produced mainly by the left ventricular myocardium in response to strain |
| <input type="radio"/> | D. Is a good marker of prognosis in patients with chronic heart failure               |
| <input type="radio"/> | E. The positive predictive value of BNP is greater than the negative predictive value |

[Next question](#)

BNP has a good negative predictive value rather than positive predictive value

#### B-type natriuretic peptide

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain.

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

#### Effects of BNP

- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

#### Clinical uses of BNP

##### Diagnosing patients with acute dyspnoea

- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis
- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure

##### Prognosis in patients with chronic heart failure

- initial evidence suggests BNP is an extremely useful marker of prognosis

## Guiding treatment in patients with chronic heart failure

- effective treatment lowers BNP levels

## Screening for cardiac dysfunction

- not currently recommended for population screening



### Question 71 of 247

One of your patients who has a family history of Marfan's syndrome has recently been diagnosed with the condition. What is the most important investigation to monitor their condition?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Urea and electrolytes |
| <input type="radio"/> | B. Echocardiography      |
| <input type="radio"/> | C. Spirometry            |
| <input type="radio"/> | D. Electrocardiogram     |
| <input type="radio"/> | E. DEXA scan             |

[Next question](#)

### Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 people.

#### Features

- tall stature with arm span to height ratio  $> 1.05$
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of  $> 20$  degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.

An elderly man with aortic stenosis is assessed. Which one of the following would make the ejection systolic murmur quieter?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Left ventricular systolic dysfunction |
| <input type="radio"/> | B. Thyrotoxicosis                        |
| <input type="radio"/> | C. Mixed aortic valve disease            |
| <input type="radio"/> | D. Expiration                            |
| <input type="radio"/> | E. Anaemia                               |

[Next question](#)

Left ventricular systolic dysfunction will result in a decreased flow-rate across the aortic valve and hence a quieter murmur.

### Aortic stenosis

#### Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

#### Causes of aortic stenosis

- degenerative calcification (most common cause in older patients > 65 years)
- bicuspid aortic valve (most common cause in younger patients < 65 years)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

#### Management

- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

An 82-year-old man is referred to cardiology by his GP with increasing dyspnoea on exertion and a systolic murmur. Examination demonstrates a blood pressure of 100/80 mmHg and a slow rising pulse. What is the most likely cause of his underlying condition?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Bicuspid aortic valve                   |
| <input type="radio"/> | B. Ventricular septal defect               |
| <input type="radio"/> | C. Post rheumatic fever                    |
| <input type="radio"/> | D. Calcification of the aortic valve       |
| <input type="radio"/> | E. Hypertrophic obstructive cardiomyopathy |

[Next question](#)

Aortic stenosis - most common cause:

- younger patients < 65 years: bicuspid aortic valve
- older patients > 65 years: calcification

This patient has aortic stenosis.

### Aortic stenosis

Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis

- degenerative calcification (most common cause in older patients > 65 years)
- bicuspid aortic valve (most common cause in younger patients < 65 years)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

## Management

- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient  $> 50$  mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Next

### Question 74 of 247

You are called to the coronary care unit. A patient who has been admitted following a myocardial infarction has developed a broad complex tachycardia. You suspect a diagnosis of polymorphic ventricular tachycardia. Which one of the following factors is most likely to have precipitated this?

- |                       |                    |
|-----------------------|--------------------|
| <input type="radio"/> | A. Hypoglycaemia   |
| <input type="radio"/> | B. Bisoprolol      |
| <input type="radio"/> | C. Hypomagnesaemia |
| <input type="radio"/> | D. Dehydration     |
| <input type="radio"/> | E. Hyperkalaemia   |

Hypokalemia is the most important cause of ventricular tachycardia (VT) clinically, followed by hypomagnesaemia. Severe hyperkalaemia may cause VT in certain circumstances, for example in patients with structural heart disease, but it is not as common a cause as hypomagnesaemia.

### Ventricular tachycardia

Ventricular tachycardia (VT) is broad-complex tachycardia originating from a ventricular ectopic focus. It has the potential to precipitate ventricular fibrillation and hence requires urgent treatment.

There are two main types of VT:

- monomorphic VT: most commonly caused by myocardial infarction
- polymorphic VT: A subtype of polymorphic VT is torsades de pointes which is precipitated by prolongation of the QT interval. The causes of a long QT interval are listed below

Causes of a prolonged QT interval

Congenital	Drugs	Other
<ul style="list-style-type: none"><li>• Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li><li>• Romano-Ward syndrome (no deafness)</li></ul>	<ul style="list-style-type: none"><li>• amiodarone, sotalol, class 1a antiarrhythmic drugs</li><li>• tricyclic antidepressants, fluoxetine</li><li>• chloroquine</li><li>• terfenadine</li><li>• erythromycin</li></ul>	<ul style="list-style-type: none"><li>• electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li><li>• acute myocardial infarction</li><li>• myocarditis</li><li>• hypothermia</li><li>• subarachnoid haemorrhage</li></ul>

### Question 75 of 247

Which one of the following features would best indicate severe aortic stenosis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Valvular gradient of 35 mmHg         |
| <input type="radio"/> | B. Quiet first heart sound              |
| <input type="radio"/> | C. Loudness of ejection systolic murmur |
| <input type="radio"/> | D. Fourth heart sound                   |
| <input type="radio"/> | E. Development of an opening snap       |

[Next question](#)

## Aortic stenosis

Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis

- degenerative calcification (most common cause in older patients > 65 years)
- bicuspid aortic valve (most common cause in younger patients < 65 years)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management

- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

[Next](#)

### Question 76 of 247

A 28-year-old man with hypertrophic obstructive cardiomyopathy is investigated for palpitations. A 24 hour ECG reveals runs of non-sustained ventricular tachycardia. What is the most appropriate management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. AV node ablation                       |
| <input type="radio"/> | B. Accessory pathway ablation             |
| <input type="radio"/> | C. Amiodarone                             |
| <input type="radio"/> | D. Implantable cardioverter defibrillator |
| <input type="radio"/> | E. Sotalol                                |

[Next question](#)

Most cardiologists would now proceed to inserting an implantable cardioverter defibrillator to lower the risk of sudden cardiac death

### HOCM: management

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

#### Management

- Amiodarone
- Beta-blockers or verapamil for symptoms
- Cardioverter defibrillator
- Dual chamber pacemaker
- Endocarditis prophylaxis\*

#### Drugs to avoid

- nitrates
- ACE-inhibitors
- inotropes

\*although see the 2008 NICE guidelines on infective endocarditis prophylaxis

A 34-year-old man is noted to have a pan-systolic murmur associated with large V waves in the JVP and pulsatile hepatomegaly. Which one of the following types of congenital heart disease is most associated with tricuspid regurgitation?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Atrial septal defect      |
| <input type="radio"/> | B. Ebstein's anomaly         |
| <input type="radio"/> | C. Coarctation of the aorta  |
| <input type="radio"/> | D. Patent ductus arteriosus  |
| <input type="radio"/> | E. Ventricular septal defect |

[Next question](#)

### Tricuspid regurgitation

#### Signs

- pan-systolic murmur
- giant V waves in JVP
- pulsatile hepatomegaly
- left parasternal heave

#### Causes

- right ventricular dilation
- pulmonary hypertension e.g. COPD
- rheumatic heart disease
- infective endocarditis (especially intravenous drug users)
- Ebstein's anomaly
- carcinoid syndrome



How long should a patient stop driving for following an elective cardiac angioplasty?

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. No restriction |
| <input type="radio"/> | B. 1 week         |
| <input type="radio"/> | C. 2 weeks        |
| <input type="radio"/> | D. 4 weeks        |
| <input type="radio"/> | E. 8 weeks        |

Next question

DVLA advice following angioplasty - cannot drive for 1 week

**The April 2009 AKT feedback report made specific mention of fitness to drive rules.**

#### **DVLA: cardiovascular disorders**

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

##### Specific rules

- hypertension - can drive unless treatment causes unacceptable side effects, no need to notify DVLA. If Group 2 Entitlement the disqualifies from driving if resting BP consistently 180 mmHg systolic or more and/or 100 mm Hg diastolic or more
- angioplasty (elective) - 1 week off driving
- CABG - 4 weeks off driving
- acute coronary syndrome- 4 weeks off driving, 1 week if successfully treated by angioplasty
- angina - driving must cease if symptoms occur at rest/at the wheel
- pacemaker insertion - 1 week off driving
- implantable cardioverter-defibrillator: if implanted for sustained ventricular arrhythmia: cease driving for 6 months. If implanted prophylatically then cease driving for 1 month
- successful catheter ablation for an arrhythmia- 2 days off driving
- aortic aneurysm of 6cm or more - notify DVLA. Licensing will be permitted subject to annual review. An aortic diameter of 6.5 cm or more disqualifies patients from driving
- heart transplant: DVLA do not need to be notified

A 56-year-old man is admitted to the Emergency Department with headaches, chest pain and confusion. His initial observations show a blood pressure of 250/140 mmHg, pulse 90/min and temperature of 36.4°. On examination the blood pressure is confirmed and is equal in both arms. Blurring of the optic discs is noted on examination. He has no significant medical history and takes no regular medications. What is the most suitable initial management?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Oral ramipril             |
| <input type="radio"/> | B. Intravenous phentolamine  |
| <input type="radio"/> | C. Venesection               |
| <input type="radio"/> | D. Intravenous nitroprusside |
| <input type="radio"/> | E. Intravenous hydralazine   |

[Next question](#)

This patient has malignant hypertension. The presence of papilloedema is an indication for the use of intravenous agents rather than slower acting oral preparations.

### Malignant hypertension

#### Basics

- severe hypertension (e.g. >200/130 mmHg)
- occurs in both essential and secondary types
- fibrinoid necrosis of blood vessels, leading to retinal haemorrhages, exudates, and proteinuria, haematuria due to renal damage (benign nephrosclerosis).
- can lead to cerebral oedema --> encephalopathy

#### Features

- classically: severe headaches, nausea/vomiting, visual disturbance
- however chest pain and dyspnoea common presenting symptoms
- papilloedema
- severe: encephalopathy (e.g. seizures)

#### Management

- reduce diastolic no lower than 100mmHg within 12-24 hrs
- bed rest
- most patients: oral therapy e.g. atenolol
- if severe/encephalopathic: IV sodium nitroprusside/labetolol

Each one of the following physiological changes occur during exercise, except:

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Increased myocardial contractibility |
| <input type="radio"/> | B. 50% increase in stroke volume        |
| <input type="radio"/> | C. Up to 3-fold increase in heart rate  |
| <input type="radio"/> | D. Rise in diastolic blood pressure     |
| <input type="radio"/> | E. Venous constriction                  |

Next question

### Exercise: physiological changes

#### Blood pressure

- systolic increases, diastolic decreases
- leads to increased pulse pressure
- in healthy young people the increase in MABP is only slight

#### Cardiac output

- increase in cardiac output may be 3-5 fold
- results from venous constriction, vasodilation and increased myocardial contractibility, as well as from the maintenance of right atrial pressure by an increase in venous return
- heart rate up to 3-fold increase
- stroke volume up to 1.5-fold increase

A 62-year-old man comes for review. In the past month he has had two episodes of 'passing out'. The first occurred whilst going upstairs. The second occurred last week whilst he was getting out of a swimming pool. There were no warning signs prior to these episodes. He was told by people who witnessed the episode last week that he was only 'out' for around 15 seconds. He reports feeling 'groggy' for only a few seconds after the episode. On examination pulse is 90 / minute, blood pressure 110/86 mmHg, his lungs are clear and there is a systolic murmur which radiates to the carotid area. Which one of the following investigations should be arranged first?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. 24 hour ECG monitor     |
| <input type="radio"/> | B. Echocardiogram          |
| <input type="radio"/> | C. Exercise tolerance test |
| <input type="radio"/> | D. CT head                 |
| <input type="radio"/> | E. Carotid doppler         |

The systolic murmur may be a pointer to aortic stenosis (AS). Syncope is a late sign and typically occurs on exertion in patients with AS. It is therefore important to exclude this condition as a priority.

An exercise tolerance test would be contraindicated in a patient with suspected aortic stenosis.

### Aortic stenosis

Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis

- degenerative calcification (most common cause in older patients > 65 years)
- bicuspid aortic valve (most common cause in younger patients < 65 years)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

## Management

- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient  $> 50$  mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Next

### Question 82 of 247

A 44-year-old female is investigated for suspected idiopathic pulmonary hypertension. Which one of the following is the best method for deciding upon management strategy?

- |                                  |   |
|----------------------------------|---|
| <input type="radio"/>            | A. Genetic testing                          |
| <input checked="" type="radio"/> | B. Acute vasodilator testing                |
| <input type="radio"/>            | C. Trial of endothelin receptor antagonists |
| <input type="radio"/>            | D. Serial echocardiography                  |
| <input type="radio"/>            | E. Trial of calcium channel blockers        |

[Next question](#)

### Pulmonary arterial hypertension: features and management

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise.

#### Features

- exertional dyspnoea is the most frequent symptom
- chest pain and syncope may also occur
- loud P2
- left parasternal heave (due to right ventricular hypertrophy)

Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy. Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide

If there is a positive response to acute vasodilator testing

- oral calcium channel blockers

If there is a negative response to acute vasodilator testing

- prostacyclin analogues: treprostinil, iloprost
- endothelin receptor antagonists: bosentan
- phosphodiesterase inhibitors: sildenafil

[Next](#)

### Question 83 of 247

Which one of the following is least associated with myocarditis?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Chagas' disease  |
| <input type="radio"/> | B. Lyme disease     |
| <input type="radio"/> | C. Leishmaniasis    |
| <input type="radio"/> | D. Cocksackie virus |
| <input type="radio"/> | E. Toxoplasmosis    |

[Next question](#)

## Myocarditis

### Causes

- viral: coxsackie, HIV
- bacteria: diphtheria, clostridia
- spirochaetes: Lyme disease
- protozoa: Chagas' disease, toxoplasmosis
- autoimmune
- drugs: doxorubicin

### Presentation

- usually young patient with acute history
- chest pain, SOB,

Which one of the following ECG findings is least associated with digoxin use?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Bradycardia                |
| <input type="radio"/> | B. Down-sloping ST depression |
| <input type="radio"/> | C. Flattened T waves          |
| <input type="radio"/> | D. Prolonged QT interval      |
| <input type="radio"/> | E. AV block                   |

Next question

### ECG: digoxin

#### ECG features

- down-sloping ST depression ('reverse tick')
- flattened/inverted T waves
- short QT interval
- arrhythmias e.g. AV block, bradycardia



Which one of the following features would indicate cardiac tamponade rather than constrictive pericarditis?

- ☐ A. Pulsus paradoxus
- ☐ B. Tachycardia
- ☐ C. Raised JVP
- ☐ D. Hypotension
- ☐ E. Muffled heart sounds

[Next question](#)

## Cardiac tamponade

### Features

- dyspnoea
- raised JVP, with an absent Y descent - this is due to the limited right ventricular filling
- tachycardia
- hypotension
- muffled heart sounds
- pulsus paradoxus
- Kussmaul's sign (much debate about this)
- ECG: electrical alternans

The key differences between constrictive pericarditis and cardiac tamponade are summarised in the table below:

	Cardiac tamponade	Constrictive pericarditis
<b>JVP</b>	Absent Y descent	X + Y present
<b>Pulsus paradoxus</b>	Present	Absent
<b>Kussmaul's sign</b>	Rare	Present
<b>Characteristic features</b>		Pericardial calcification on CXR

A commonly used mnemonic to remember the absent Y descent in cardiac tamponade is TAMponade = TAMpaX

You are asked to urgently review a 61-year-old female on the cardiology ward due to difficulty in breathing. On examination she has a raised JVP with bilateral fine crackles to the mid zones. Blood pressure is 94/60 mmHg and the pulse is 140-150 and irregular. ECG confirms atrial fibrillation. What is the most appropriate management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. IV amiodarone                        |
| <input type="radio"/> | B. IV digoxin                           |
| <input type="radio"/> | C. Urgent synchronised DC cardioversion |
| <input type="radio"/> | D. Oral digoxin                         |
| <input type="radio"/> | E. IV flecainide                        |

[Next question](#)

Heart failure is one of the adverse signs indicating the need for urgent synchronised DC cardioversion

### Peri-arrest rhythms: tachycardia

The 2010 Resuscitation Council (UK) guidelines have simplified the advice given for the management of peri-arrest tachycardias. Separate algorithms for the management of broad-complex tachycardia, narrow complex tachycardia and atrial fibrillation have been replaced by one unified treatment algorithm

Following basic ABC assessment, patients are classified as being stable or unstable according to the presence of any adverse signs:

- shock: hypotension (systolic blood pressure < 90 mmHg), pallor, sweating,

cold, clammy extremities, confusion or impaired consciousness

- syncope
- myocardial ischaemia
- heart failure

If any of the above adverse signs are present then synchronised DC shocks should be given

Treatment following this is given according to whether the QRS complex is narrow or broad and whether the rhythm is regular or irregular. The full treatment algorithm can be found at the Resuscitation Council website, below is a very limited summary:

### Broad-complex tachycardia

Regular

- assume ventricular tachycardia (unless previously confirmed SVT with bundle branch block)

- loading dose of amiodarone followed by 24 hour infusion

Irregular

- 1. AF with bundle branch block - treat as for narrow complex tachycardia
- 2. Polymorphic VT (e.g. Torsade de pointes) - IV magnesium

### **Narrow-complex tachycardia**

Regular

- vagal manoeuvres followed by IV adenosine
- if above unsuccessful consider diagnosis of atrial flutter and control rate (e.g. Beta-blockers)

Irregular

- probable atrial fibrillation
- if onset < 48 hr consider electrical or chemical cardioversion
- rate control (e.g. Beta-blocker or digoxin) and anticoagulation

Pulmonary arterial hypertension may be seen in each one of the following conditions, except:

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Hepatitis B            |
| <input type="radio"/> | B. Eisenmenger's syndrome |
| <input type="radio"/> | C. Sickle cell anaemia    |
| <input type="radio"/> | D. HIV                    |
| <input type="radio"/> | E. Sarcoidosis            |

Next question

Hepatitis B is not a recognised cause of pulmonary arterial hypertension

### **Pulmonary arterial hypertension: causes and classification**

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise. PAH has recently been reclassified by the WHO:

Group 1: Pulmonary arterial hypertension (PAH)

- idiopathic\*
- familial
- associated conditions: collagen vascular disease, congenital heart disease with systemic to pulmonary shunts, HIV\*\*, drugs and toxins, sickle cell disease
- persistent pulmonary hypertension of the newborn

Group 2: Pulmonary hypertension with left heart disease

- left-sided atrial, ventricular or valvular disease such as left ventricular systolic and diastolic dysfunction, mitral stenosis and mitral regurgitation

Group 3: Pulmonary hypertension secondary to lung disease/hypoxia

- COPD
- interstitial lung disease
- sleep apnoea
- high altitude

Group 4: Pulmonary hypertension due to thromboembolic disease

Group 5: Miscellaneous conditions

- lymphangiomatosis e.g. secondary to carcinomatosis or sarcoidosis

\*previously termed primary pulmonary hypertension

\*\*the mechanism by which HIV infection produces pulmonary hypertension remains unknown

A 43-year-old man who is known to have Wolff-Parkinson White syndrome presents to the Emergency Department with palpitations. He has no other significant history of note. The palpitations started around 4 hours ago and are not associated with chest pain or shortness of breath. On examination blood pressure is 124/80 mmHg and the chest is clear on auscultation. An ECG show atrial fibrillation at a rate of 154 bpm. Of the following options, what is the most appropriate management?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Adenosine  |
| <input type="radio"/> | B. Flecainide |
| <input type="radio"/> | C. Verapamil  |
| <input type="radio"/> | D. Digoxin    |
| <input type="radio"/> | E. Sotalol    |

[Next question](#)

Adenosine should be avoided as blocking the AV node can paradoxically increase ventricular rate resulting in fall in cardiac output. Verapamil and digoxin should also be avoided in patients with Wolff-Parkinson White as they may precipitate VT or VF.

Another option to consider in this situation would be DC cardioversion

### Wolff-Parkinson White

Wolff-Parkinson White (WPW) syndrome is caused by a congenital accessory conducting pathway between the atria and ventricles leading to a atrioventricular re-entry tachycardia (AVRT). As the accessory pathway does not slow conduction AF can degenerate rapidly to VF

Possible ECG features include:

- short PR interval
- wide QRS complexes with a slurred upstroke - 'delta wave'
- left axis deviation if right-sided accessory pathway\*
- right axis deviation if left-sided accessory pathway\*

Differentiating between type A and type B

- type A (left-sided pathway): dominant R wave in V1
- type B (right-sided pathway): no dominant R wave in V1

Associations of WPW

- HOCM
- mitral valve prolapse

- Ebstein's anomaly
- thyrotoxicosis
- secundum ASD

## Management

- definitive treatment: radiofrequency ablation of the accessory pathway
- medical therapy: sotalol\*\*, amiodarone, flecainide

\*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

\*\*sotalol should be avoided if there is coexistent atrial fibrillation as prolonging the refractory period at the AV node may increase the rate of transmission through the accessory pathway, increasing the ventricular rate and potentially deteriorating into ventricular fibrillation

A 62-year-old man is admitted to hospital following a myocardial infarction. Four days after admission he develops a further episode of central crushing chest pain. Which is the best cardiac marker to investigate his chest pain?

- ☐ A. LDH
- ☐ B. Troponin I
- ☐ C. Troponin T
- ☐ D. CK-MB
- ☐ E. AST

Next question

By day four the CK-MB levels should have returned to normal from the initial myocardial infarction. If the CK-MB levels are elevated it would indicate a further coronary event

### Cardiac enzymes and protein markers

Interpretation of the various cardiac enzymes has now largely been superseded by the introduction of troponin T and I. Questions still however commonly appear in the MRCP

Key points for the exam

- myoglobin is the first to rise
- CK-MB is useful to look for reinfarction as it returns to normal after 2-3 days (troponin T remains elevated for up to 10 days)

	Begins to rise	Peak value	Returns to normal
<b>Myoglobin</b>	1-2 hours	6-8 hours	1-2 days
<b>CK-MB</b>	2-6 hours	16-20 hours	2-3 days
<b>CK</b>	4-8 hours	16-24 hours	3-4 days
<b>Trop T</b>	4-6 hours	12-24 hours	7-10 days
<b>AST</b>	12-24 hours	36-48 hours	3-4 days
<b>LDH</b>	24-48 hours	72 hours	8-10 days

Which one of the following is a cause of a soft second heart sound?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Aortic stenosis        |
| <input type="radio"/> | B. Aortic regurgitation   |
| <input type="radio"/> | C. Mitral stenosis        |
| <input type="radio"/> | D. Mitral regurgitation   |
| <input type="radio"/> | E. Pulmonary hypertension |

Next question

#### Second heart sound (S2)

- loud: hypertension
- soft: AS
- fixed split: ASD
- reversed split: LBBB

S2 is soft in severe aortic stenosis

#### Heart sounds: S2

S2 is caused by the closure of the aortic valve (A2) closely followed by that of the pulmonary valve (P2)

#### Causes of a loud S2

- hypertension: systemic (loud A2) or pulmonary (loud P2)
- hyperdynamic states
- atrial septal defect without pulmonary hypertension

#### Causes of a soft S2

- aortic stenosis

#### Causes of fixed split S2

- atrial septal defect

#### Causes of a widely split S2



- deep inspiration
- RBBB
- pulmonary stenosis
- severe mitral regurgitation

Causes of a reversed (paradoxical) split S2 (P2 occurs before A2)

- LBBB
- severe aortic stenosis
- right ventricular pacing
- WPW type B (causes early P2)
- patent ductus arteriosus

### Question 91 of 247

A 72-year-old man with a history of chronic heart failure secondary to ischaemic cardiomyopathy is reviewed. He was discharged two weeks ago from hospital following a myocardial infarction. An echocardiogram done during his admission showed a left ventricular ejection fraction of 40% but did not demonstrate any valvular problems.

Despite his current treatment with furosemide, ramipril, carvedilol, aspirin and simvastatin he remains short of breath on minimal exertion such as walking 30 metres. On examination his chest is clear and there is minimal peripheral oedema. What is the most appropriate next step in management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Stop aspirin                                |
| <input type="radio"/> | B. Refer for cardiac resynchronisation therapy |
| <input type="radio"/> | C. Switch carvedilol to bisoprolol             |
| <input type="radio"/> | D. Add angiotensin-2 receptor blocker          |
| <input type="radio"/> | E. Add an aldosterone antagonist               |

[Next question](#)

The updated 2010 NICE guidelines now suggest that in addition to aldosterone antagonists both angiotensin-2 receptor blockers and hydralazine in combination with a nitrate are suitable second-line treatments for heart failure. However, given that he has had a recent myocardial infarction the best choice is an aldosterone antagonist - please see the NICE guidelines for more details.

### Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:

- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:

- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin\* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off\*\* pneumococcal vaccine

\*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

\*\*adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years

**Question 92 of 247**

A 76-year-old female is admitted after being found on the floor at her home. On examination she has a core temperature of 30°C. Her serum electrolytes are within normal range. Which one of the ECG findings is most likely to be seen?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Long QT interval          |
| <input type="radio"/> | B. 'U' waves                 |
| <input type="radio"/> | C. Short PR interval         |
| <input type="radio"/> | D. Second degree heart block |
| <input type="radio"/> | E. Flattened T waves         |

**ECG: hypothermia**

The following ECG changes may be seen in hypothermia

- bradycardia
- 'J' wave - small hump at the end of the QRS complex
- first degree heart block
- long QT interval
- atrial and ventricular arrhythmias

### Question 93 of 247

A 62-year-old man is reviewed. His blood pressure is poorly controlled at 152/90 mmHg despite treatment with ramipril 10mg od, bendroflumethiazide 2.5mg od and amlodipine 10mg od. In addition to the antihypertensives he also takes aspirin and simvastatin. His most recent blood tests show the following:

Na <sup>+</sup>	139 mmol/l
K <sup>+</sup>	4.2 mmol/l
Urea	5.5 mmol/l
Creatinine	98 µmol/l

What is the most appropriate change to his medication?

- ☐ A. Add frusemide
- ☐ B. Increase ramipril to 20mg od
- ☐ C. Add spironolactone
- ☐ D. Add candesartan
- ☐ E. Add atenolol

[Next question](#)

#### Hypertension - step 4

- K<sup>+</sup> < 4.5 then spironolactone
- K<sup>+</sup> > 4.5 then higher-dose thiazide-like diuretic

This patient has reached step 4 in the NICE hypertension guidelines. As their potassium is less than 4.5 mmol/l spironolactone 25mg od should be started.

#### Hypertension: diagnosis and management

NICE published updated guidelines for the management of hypertension in 2011. Some of the key changes include:

- classifying hypertension into stages
- recommending the use of ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM)
- calcium channel blockers are now considered superior to thiazides
- bendroflumethiazide is no longer the thiazide of choice

#### Blood pressure classification

This becomes relevant later in some of the management decisions that NICE advocate.

<b>Stage 1 hypertension</b>	Clinic BP $\geq$ 140/90 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 135/85 mmHg
<b>Stage 2 hypertension</b>	Clinic BP $\geq$ 160/100 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 150/95 mmHg
<b>Severe hypertension</b>	Clinic systolic BP $\geq$ 180 mmHg, or clinic diastolic BP $\geq$ 110 mmHg

## Diagnosing hypertension

If a BP reading is  $\geq$  140 / 90 mmHg patients should be offered ABPM to confirm the diagnosis.

Patients with a BP reading of  $\geq$  180/110 mmHg should be considered for immediate treatment.

Ambulatory blood pressure monitoring (ABPM)

- at least 2 measurements per hour during the person's usual waking hours (for example, between 08:00 and 22:00)
- use the average value of at least 14 measurements

If ABPM is not tolerated or declined HBPM should be offered.

Home blood pressure monitoring (HBPM)

- for each BP recording, two consecutive measurements need to be taken, at least 1 minute apart and with the person seated
- BP should be recorded twice daily, ideally in the morning and evening
- BP should be recorded for at least 4 days, ideally for 7 days
- discard the measurements taken on the first day and use the average value of all the remaining measurements

## Managing hypertension

ABPM/HBPM  $\geq$  135/85 mmHg (i.e. stage 1 hypertension)

- treat if  $<$  80 years of age and any of the following apply; target organ damage, established cardiovascular disease, renal disease, diabetes or a 10-year cardiovascular risk equivalent to 20% or greater

ABPM/HBPM  $\geq$  150/95 mmHg (i.e. stage 2 hypertension)

- offer drug treatment regardless of age

For patients  $<$  40 years consider specialist referral to exclude secondary causes.

Step 1 treatment

- patients  $<$  55-years-old: ACE inhibitor (A)
- patients  $>$  55-years-old or of Afro-Caribbean origin: calcium channel blocker

## Step 2 treatment

- ACE inhibitor + calcium channel blocker (A + C)

## Step 3 treatment

- add a thiazide diuretic (D, i.e. A + C + D)
- NICE now advocate using either chlorthalidone (12.5-25.0 mg once daily) or indapamide (1.5 mg modified-release once daily or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide

NICE define a clinic BP  $\geq 140/90$  mmHg after step 3 treatment with optimal or best tolerated doses as resistant hypertension. They suggest step 4 treatment or seeking expert advice

## Step 4 treatment

- consider further diuretic treatment
- if potassium  $< 4.5$  mmol/l add spironolactone 25mg od
- if potassium  $> 4.5$  mmol/l add higher-dose thiazide-like diuretic treatment
- if further diuretic therapy is not tolerated, or is contraindicated or ineffective, consider an alpha- or beta-blocker

If BP still not controlled seek specialist advice.

## Blood pressure targets

	Clinic BP	ABPM / HBPM
Age $< 80$ years	140/90 mmHg	135/85 mmHg
Age $> 80$ years	150/90 mmHg	145/85 mmHg

## New drugs

### Direct renin inhibitors

- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

A patient with known heart failure has slight limitation of physical activity. She is comfortable at rest but housework results in fatigue, palpitations or dyspnoea. What New York Heart Association class best describes the severity of their disease?

<input type="radio"/>	A. NYHA Class 0
<input type="radio"/>	B. NYHA Class I
<input type="radio"/>	C. NYHA Class II
<input type="radio"/>	D. NYHA Class III
<input type="radio"/>	E. NYHA Class IV

[Next question](#)

### Heart failure: NYHA classification

The New York Heart Association (NYHA) classification is widely used to classify the severity of heart failure:

#### NYHA Class I

- no symptoms
- no limitation: ordinary physical exercise does not cause undue fatigue, dyspnoea or palpitations

#### NYHA Class II

- mild symptoms
- slight limitation of physical activity: comfortable at rest but ordinary activity results in fatigue, palpitations or dyspnoea

#### NYHA Class III

- moderate symptoms
- marked limitation of physical activity: comfortable at rest but less than ordinary activity results in symptoms

#### NYHA Class IV

- severe symptoms
- unable to carry out any physical activity without discomfort: symptoms of heart failure are present even at rest with increased discomfort with any physical activity



A 51-year-old female presents to the Emergency Department following an episode of transient right sided weakness lasting 10-15 minutes. Examination reveals the patient to be in atrial fibrillation. If the patient remains in chronic atrial fibrillation what is the most suitable form of anticoagulation?

- ☐ A. Aspirin
- ☐ B. Warfarin, target INR 2-3
- ☐ C. No anticoagulation
- ☐ D. Warfarin, target INR 3-4
- ☐ E. Warfarin, target INR 2-3 for six months then aspirin

Next question

The CHA<sub>2</sub>DS<sub>2</sub>-VASc for this patient is 3 - 2 for the transient ischaemic attack and 1 for being female. She should therefore be offered anticoagulation with warfarin.

### Atrial fibrillation: anticoagulation

The European Society of Cardiology published updated guidelines on the management of atrial fibrillation in 2012. They suggest using the **CHA<sub>2</sub>DS<sub>2</sub>-VASc** score to determine the most appropriate anticoagulation strategy. This scoring system superseded the CHADS<sub>2</sub> score.

	Condition	Points
<b>C</b>	Congestive heart failure	1
<b>H</b>	Hypertension (or treated hypertension)	1
<b>A<sub>2</sub></b>	Age ≥ 75 years	2
<b>D</b>	Diabetes	1
<b>S<sub>2</sub></b>	Prior Stroke or TIA	2
<b>V</b>	Vascular disease (including ischaemic heart disease and peripheral arterial disease)	1
<b>A</b>	Age 65-74 years	1
<b>S</b>	Sex (female)	1

The table below shows a suggested anticoagulation strategy\* based on the score:

Score	Anticoagulation
0	No treatment is preferred to aspirin
1	Oral anticoagulants preferred to aspirin; dabigatran is an alternative
2 or more	Oral anticoagulants; dabigatran is an alternative

\*the wording in the guidelines ('is preferred to') can be slightly confusing. It basically means that, say for a score of 0, whilst aspirin is an acceptable management option the weight of the clinical evidence would support no treatment instead

A 52-year-old man with no significant past medical history is admitted to the Emergency Department with chest pain. His admission ECG shows anterior T wave inversion. On examination his blood pressure is 120/82 mmHg, pulse 90 / min and oxygen saturations are 97% on room air. He is now pain free. You calculate his 6 month mortality using GRACE to be 1.0%. What initial therapy should be given?

- ☐ A. Oxygen + aspirin + enoxaparin
- ☐ B. Aspirin + unfractionated heparin
- ☐ C. Oxygen + aspirin + clopidogrel + enoxaparin
- ☐ D. Aspirin + fondaparinux
- ☐ E. Aspirin

[Next question](#)

The NICE guidelines would advocate the use of fondaparinux in this scenario. Given the clinical details in this case it is unlikely that angiography will be performed in the next 24 hours and hence unfractionated heparin is not required.

### Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive

- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

**Antithrombin** treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is > 265  $\mu\text{mol/l}$  unfractionated heparin should be given.

**Clopidogrel** 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

**Coronary angiography** should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

<b>Aspirin</b>	Antiplatelet - inhibits the production of thromboxane A2
<b>Clopidogrel</b>	Antiplatelet - inhibits ADP binding to its platelet receptor
<b>Enoxaparin</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Fondaparinux</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Bivalirudin</b>	Reversible direct thrombin inhibitor

### Question 97 of 247

In patients with atrial fibrillation (AF), which one of the following factors would make a rate control strategy, rather than rhythm control, more suitable?

- ☐ A. Congestive heart failure
- ☐ B. AF secondary to a corrected precipitant
- ☐ C. Symptomatic
- ☐ D. Age > 65 years
- ☐ E. First presentation

[Next question](#)

### Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
Older than 65 years History of ischaemic heart disease	Younger than 65 years Symptomatic First presentation

	Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) Congestive heart failure
--	---

### Question 98 of 247

A 23-year-old woman is investigated after collapsing whilst jogging. She felt briefly unwell and dizzy prior to collapsing but quickly recovered. There has been no previous similar episodes. Routine blood tests are normal but the ECG shows a corrected QT interval of 480ms. What is the most appropriate management?

- ☐ A. Implantable cardioverter defibrillator
- ☐ B. Propranolol
- ☐ C. Amiodarone
- ☐ D. Reassurance
- ☐ E. Accessory pathway ablation

[Next question](#)

An implantable cardioverter defibrillator is only required in high risk cases, for example if the patient has a QTc > 500ms or previous episodes of cardiac arrest.

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"><li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li><li>Romano-Ward syndrome (no deafness)</li></ul>	<ul style="list-style-type: none"><li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li><li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li><li>methadone</li><li>chloroquine</li><li>terfenadine**</li><li>erythromycin</li></ul>	<ul style="list-style-type: none"><li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li><li>acute myocardial infarction</li><li>myocarditis</li><li>hypothermia</li><li>subarachnoid haemorrhage</li></ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

## Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

Next

### Question 99 of 247

Which of the following is least associated with mitral valve prolapse?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Osteogenesis imperfecta  |
| <input type="radio"/> | B. Pseudoxanthoma elasticum |
| <input type="radio"/> | C. Turner's syndrome        |
| <input type="radio"/> | D. Marfan's syndrome        |
| <input type="radio"/> | E. Acromegaly               |

[Next question](#)

Whilst some patients with acromegaly have mitral valve prolapse (MVP) it is not a common association. It should be remembered that the prevalence of MVP in a standard population is around 5-10%

### Mitral valve prolapse

Mitral valve prolapse is common, occurring in around 5-10 % of the population. It is usually idiopathic but may be associated with a wide variety of cardiovascular disease and other conditions

#### Associations

- congenital heart disease: PDA, ASD
- cardiomyopathy
- Turner's syndrome
- Marfan's syndrome, Fragile X
- osteogenesis imperfecta
- pseudoxanthoma elasticum
- Wolff-Parkinson White syndrome
- long-QT syndrome
- Ehlers-Danlos Syndrome
- polycystic kidney disease

#### Features

- patients may complain of atypical chest pain or palpitations
- mid-systolic click (occurs later if patient squatting)
- late systolic murmur (longer if patient standing)
- complications: mitral regurgitation, arrhythmias (including long QT), emboli, sudden death

[Next](#)



### Question 100 of 247

A 54-year-old man with angina has a percutaneous coronary intervention with insertion of a drug-eluting stent. What is the single most important risk factor for stent thrombosis?

- ☐ A. Age of patient
- ☐ B. Premature withdrawal of antiplatelet therapy
- ☐ C. Failing to adhere to cardiac rehabilitation program
- ☐ D. Duration of procedure
- ☐ E. History of diabetes mellitus

Next question

PCI: stent thrombosis - withdrawal of antiplatelets biggest risk factor

Diabetes mellitus is a risk factor for restenosis rather than stent thrombosis

### Percutaneous coronary intervention

Percutaneous coronary intervention (PCI) is a technique used to restore myocardial perfusion in patients with ischaemic heart disease, both in patients with stable angina and acute coronary syndromes. Stents are implanted in around 95% of patients - it is now rare for just balloon angioplasty to be performed

Following stent insertion migration and proliferation of smooth muscle cells and fibroblasts occur to the treated segment. The stent struts eventually become covered by endothelium. Until this happens there is an increased risk of platelet aggregation leading to thrombosis.

Two main complications may occur

- stent thrombosis: due to platelet aggregation as above. Occurs in 1-2% of patients, most commonly in the first month. Usually presents with acute myocardial infarction
- restenosis: due to excessive tissue proliferation around stent. Occurs in around 5-20% of patients, most commonly in the first 3-6 months. Usually presents with the recurrence of angina symptoms. Risk factors include diabetes, renal impairment and stents in venous bypass grafts

Types of stent

- bare-metal stent (BMS)
- drug-eluting stents (DES): stent coated with paclitaxel or rapamycin which inhibit local tissue growth. Whilst this reduces restenosis rates the stent thrombosis rates are increased as the process of stent endothelialisation is slowed

Following insertion the most important factor in preventing stent thrombosis is antiplatelet therapy. Aspirin should be continued indefinitely. The length of clopidogrel treatment depends on the type of stent, reason for insertion and consultant preference

Which one of the following complications is least associated with ventricular septal defects?

<input type="radio"/>	A. Right heart failure
<input type="radio"/>	B. Aortic regurgitation
<input type="radio"/>	C. Eisenmenger's complex
<input type="radio"/>	D. Infective endocarditis
<input type="radio"/>	E. Atrial fibrillation

Next question

Atrial fibrillation is associated more with atrial septal defects

### Ventricular septal defects

Ventricular septal defects are the most common cause of congenital heart disease. They close spontaneously in around 50% of cases. Non-congenital causes include post myocardial infarction

#### Features

- classically a pan-systolic murmur which is louder in smaller defects

#### Complications

- aortic regurgitation\*
- infective endocarditis
- Eisenmenger's complex
- right heart failure

\*aortic regurgitation is due to a poorly supported right coronary cusp resulting in cusp prolapse

A 23-year-old man with a family history of sudden cardiac death is diagnosed as having hypertrophic obstructive cardiomyopathy. Which one of the following is the strongest marker of poor prognosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Mitral regurgitation  |
| <input type="radio"/> | B. Apical hypertrophy  |
| <input type="radio"/> | C. Systolic anterior motion of the anterior mitral valve leaflet |
| <input type="radio"/> | D. Septal wall thickness of > 3cm                                |
| <input type="radio"/> | E. Asymmetric hypertrophy  |

[Next question](#)

HOCM - poor prognostic factor on echo = septal wall thickness of > 3cm

### HOCM: prognostic factors

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. Mutations to various proteins including beta-myosin, alpha-tropomyosin and troponin T have been identified. Septal hypertrophy causes left ventricular outflow obstruction. It is an important cause of sudden death in apparently healthy individuals.

Poor prognostic factors

- syncope
- family history of sudden death
- young age at presentation
- non-sustained ventricular tachycardia on 24 or 48-hour Holter monitoring
- abnormal blood pressure changes on exercise

An increased septal wall thickness is also associated with a poor prognosis.

A 65-year-old man with no significant past medical history is admitted to the Emergency Department. His ECG is consistent with an anterior myocardial infarction. Unfortunately he develops cardiac arrest shortly after arriving in the department. What is the most common cause of death in patients following a myocardial infarction?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Pulmonary embolism       |
| <input type="radio"/> | B. Cardiogenic shock        |
| <input type="radio"/> | C. Papillary muscle rupture |
| <input type="radio"/> | D. Ventricular fibrillation |
| <input type="radio"/> | E. Complete heart block     |

[Next question](#)

### Myocardial infarction: complications

Patients are at risk of a number of immediate, early and late complications following a myocardial infarction (MI).

#### Cardiac arrest

This most commonly occurs due to patients developing and is the most common cause of death following a MI. Patients are managed as per the ALS protocol with defibrillation.

#### Cardiogenic shock

If a large part of the ventricular myocardium is damaged in the infarction the ejection fraction of the heart may decrease to the point that the patient develops cardiogenic shock. This is difficult to treat. Other causes of cardiogenic shock include the 'mechanical' complications such as left ventricular free wall rupture as listed below. Patients may require inotropic support and/or an intra-aortic balloon pump.

#### Chronic heart failure

As described above, if the patient survives the acute phase their ventricular myocardium may be dysfunctional resulting in chronic heart failure. Loop diuretics such as furosemide will decrease fluid overload. Both ACE-inhibitors and beta-blockers have been shown to improve the long-term prognosis of patients with chronic heart failure.

#### Tachyarrhythmias

Ventricular fibrillation, as mentioned above, is the most common cause of death following a MI. Other common arrhythmias including ventricular tachycardia.

#### Bradyarrhythmias

Atrioventricular block is more common following inferior myocardial infarctions.

### **Pericarditis**

Pericarditis in the first 48 hours following a transmural MI is common (c. 10% of patients). The pain is typical for pericarditis (worse on lying flat etc), a pericardial rub may be heard and a pericardial effusion may be demonstrated with an echocardiogram.

Dressler's syndrome tends to occur around 2-6 weeks following a MI. The underlying pathophysiology is thought to be an autoimmune reaction against antigenic proteins formed as the myocardium recovers. It is characterised by a combination of fever, pleuritic pain, pericardial effusion and a raised ESR. It is treated with NSAIDs.

### **Left ventricular aneurysm**

The ischaemic damage sustained may weaken the myocardium resulting in aneurysm formation. This is typically associated with persistent ST elevation and left ventricular failure. Thrombus may form within the aneurysm increasing the risk of stroke. Patients are therefore anticoagulated.

### **Left ventricular free wall rupture**

This is seen in around 3% of MIs and occurs around 1-2 weeks afterwards. Patients present with acute heart failure secondary to cardiac tamponade (raised JVP, pulsus paradoxus, diminished heart sounds). Urgent pericardiocentesis and thoracotomy are required.

### **Ventricular septal defect**

Rupture of the interventricular septum usually occurs in the first week and is seen in around 1-2% of patients. Features: acute heart failure associated with a pan-systolic murmur. An echocardiogram is diagnostic and will exclude acute mitral regurgitation which presents in a similar fashion. Urgent surgical correction is needed.

### **Acute mitral regurgitation**

More common with infero-posterior infarction and may be due to ischaemia or rupture of the papillary muscle. An early-to-mid systolic murmur is typically heard. Patients are treated with vasodilator therapy but often require emergency surgical repair.

A 62-year-old man is admitted with pyrexia and found to have infective endocarditis. Which one of the following is most associated with a good prognosis?

- ☐ A. *Staphylococcus aureus* infection
- ☐ B. Culture negative endocarditis
- ☐ C. *Streptococcus viridans* infection
- ☐ D. Low complement levels
- ☐ E. Prosthetic valve endocarditis

[Next question](#)

Infective endocarditis - streptococcal infection carries a good prognosis

### Infective endocarditis: prognosis and management

Poor prognostic factors

- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism

- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)

Scenario	Suggested antibiotic therapy
Initial blind therapy	Flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
Initial blind therapy if prosthetic valve is present or patient is penicillin allergic	Vancomycin + rifampicin + gentamicin
Endocarditis caused by staphylococci	Flucloxacillin (add rifampicin if prosthetic valve, vancomycin + rifampicin if penicillin allergic or MRSA)
Native valve endocarditis caused by fully-sensitive streptococci	Benzylpenicillin (large vegetation, intracardial abscess or infected emboli then

(e.g. viridans)	benzylpenicillin + gentamicin, vancomycin if penicillin allergic)
Native valve endocarditis caused by less sensitive streptococci OR prosthetic valve endocarditis caused by streptococci	Benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

#### Indications for surgery

- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy



You are called to assess a man who has collapsed in the clinic waiting room. A staff nurse has already bleeped the cardiac arrest team. On arrival the man is laid on his back. You open the airway with a head-tilt chin lift - after assessing for 10 seconds there are no signs of breathing. What is the most appropriate next step?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Start chest compressions at a ratio of 15:2 |
| <input type="radio"/> | B. Place in the recovery position              |
| <input type="radio"/> | C. Check for a carotid pulse for 10 seconds    |
| <input type="radio"/> | D. Give 2 rescue breaths                       |
| <input type="radio"/> | E. Start chest compressions at a ratio of 30:2 |

Next question

The 2010 guidelines do not support the concept of 'checking for circulation'; absence of breathing, in a non-responsive individual, is now used as the main sign of cardiac arrest. In reality most medical professionals will check for a carotid pulse whilst assessing breathing, but in this scenario to wait a further 10 seconds before starting chest compressions is not justifiable. Please see the link to the BLS guidelines.

### Adult advanced life support

The joint European Resuscitation Council and Resuscitation Council (UK) 2010 guidelines do not alter significantly from the 2005 guidelines. Please see the link for more details, below is only a very brief summary of key points / changes.

Major points include:

- ratio of chest compressions to ventilation is 30:2
- chest compressions are now continued while a defibrillator is charged
- during a VF/VT cardiac arrest, adrenaline 1 mg is given once chest compressions have restarted after the third shock and then every 3-5 minutes (during alternate cycles of CPR). In the 2005 guidelines, adrenaline was given just before the third shock. Amiodarone 300 mg is also given after the third shock
- atropine is no longer recommended for routine use in asystole or pulseless

electrical activity (PEA).

- a single shock for VF/pulseless VT followed by 2 minutes of CPR, rather than a series of 3 shocks followed by 1 minute of CPR
- asystole/pulseless-electrical activity should be treated with 2 minutes of CPR, rather than 3, prior to reassessment of the rhythm
- delivery of drugs via a tracheal tube is no longer recommended
- following successful resuscitation oxygen should be titrated to achieve saturations of 94-98%. This is to address the potential harm caused by hyperoxaemia

Which part of the jugular venous waveform may be exaggerated in tricuspid regurgitation?

<input type="radio"/>	A. x descent
<input checked="" type="radio"/>	B. v wave
<input type="radio"/>	C. y descent
<input type="radio"/>	D. a wave
<input type="radio"/>	E. c wave

Next question

JVP: giant v waves in tricuspid regurgitation

### Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis.

'a' wave = atrial contraction

- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves

- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave

- closure of tricuspid valve
- not normally visible

'v' wave

- due to passive filling of blood into the atrium against a closed tricuspid valve
- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve

A 72-year-old male is admitted to the Emergency Room following a collapse at church. ECG reveals dissociation between the P and QRS complexes with a rate of 40 / minute. Which one of the following clinical findings may also be found?

<input type="radio"/>	A. Loud S1
<input type="radio"/>	B. Narrow pulse pressure
<input type="radio"/>	C. Giant v waveforms in the JVP
<input type="radio"/>	D. Variable intensity of S1
<input type="radio"/>	E. Soft S2

[Next question](#)

### Complete heart block

#### Features

- syncope
- heart failure
- regular bradycardia (30-50 bpm)
- wide pulse pressure
- JVP: cannon waves in neck
- variable intensity of S1

### Question 108 of 247

A 61-year-old woman who is normally fit and well is admitted with chest pain. An ECG shows anterolateral T wave inversion. The troponin T value at 12 hours is 0.54. On discharge her medications include aspirin, atorvastatin, bisoprolol and ramipril. Which one of the following statements best describes the role of clopidogrel in this situation?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Is only given if aspirin is contraindicated   |
| <input type="radio"/> | B. Should be prescribed for life for patients < 65 years old   |
| <input type="radio"/> | C. Should be prescribed for the next 12 months for patients who have a 6 month mortality risk of greater than 1.5% |
| <input type="radio"/> | D. Should be prescribed for the next 12 months for patients < 65 years old   |
| <input type="radio"/> | E. Should be prescribed for the next 12 months for patients who have a 12 month mortality risk of greater than 5%  |

[Next question](#)

NICE NSTEMI/unstable angina guidelines are based on 6 month mortality risk:

- if > 1.5% clopidogrel for 12 months
- if > 3% angiography within 96 hours

Please see the 2010 NICE unstable angina and NSTEMI guidelines for more details. The 6 month mortality may be calculated using a risk model such as GRACE.

### Myocardial infarction: secondary prevention

NICE produced guidelines on the management of patients following a myocardial infarction (MI) in 2007. Some key points are listed below

All patients should be offered the following drugs:

- ACE inhibitor
- beta-blocker
- aspirin
- statin

### Clopidogrel

- ST-segment-elevation MI: patients treated with a combination of aspirin and clopidogrel during the first 24 hours after the MI should continue this treatment for at least 4 weeks

- non-ST segment elevation myocardial infarction (NSTEMI): following the 2010 NICE unstable angina and NSTEMI guidelines clopidogrel should be given for the first 12 months if the 6 month mortality risk\* is > 1.5%

#### Aldosterone antagonists

- patients who have had an acute MI and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, treatment with an aldosterone antagonist licensed for post-MI treatment (e.g. eplerenone) should be initiated within 3-14 days of the MI, preferably after ACE inhibitor therapy

\*this can be calculated using scoring systems such as GRACE

Next

### Question 109 of 247

Which one of the following is least likely to cause dilated cardiomyopathy?

<input type="radio"/>	A. Wilson's disease
<input type="radio"/>	B. Haemochromatosis
<input type="radio"/>	C. Cocksackie A
<input type="radio"/>	D. Hypertension
<input type="radio"/>	E. Alcohol

Haemochromatosis is more commonly associated with restrictive cardiomyopathy but a dilated pattern may also be seen. There is a known association between Wilson's disease and cardiomyopathy but this is extremely rare and not often clinically significant

### Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) basics

- dilated heart leading to systolic (+/- diastolic) dysfunction
- all 4 chambers affected but LV more so than RV
- features include arrhythmias, emboli, mitral regurgitation
- absence of congenital, valvular or ischaemic heart disease

Causes often considered separate entities

- alcohol: may improve with thiamine
- postpartum
- hypertension

Other causes

- inherited (see below)
- infections e.g. Cocksackie A and B, HIV, diphtheria, parasitic
- endocrine e.g. Hyperthyroidism
- infiltrative\* e.g. Haemochromatosis, sarcoidosis
- neuromuscular e.g. Duchenne muscular dystrophy
- nutritional e.g. Kwashiorkor, pellagra, thiamine/selenium deficiency
- drugs e.g. Doxorubicin

Inherited dilated cardiomyopathy

- around a third of patients with DCM are thought to have a genetic predisposition
- a large number of heterogeneous defects have been identified
- the majority of defects are inherited in an autosomal dominant fashion although other patterns of inheritance are seen

\*these causes may also lead to restrictive cardiomyopathy

Each one of the following is associated with atrial myxoma, except:

<input type="radio"/>	A. Clubbing
<input type="radio"/>	B. Mid-diastolic murmur
<input type="radio"/>	C. Pyrexia
<input checked="" type="radio"/>	D. 'J' wave on ECG
<input type="radio"/>	E. Atrial fibrillation

[Next question](#)

A 'J' wave is seen in hypothermia

## Atrial myxoma

### Overview

- 75% occur in left atrium
- more common in females

### Features

- systemic: weight loss, fever, clubbing
- emboli
- atrial fibrillation
- mid-diastolic murmur, 'tumour plop'

### Question 111 of 247

A 71-year-old woman is admitted with acute dyspnoea to the Emergency Department. Oxygen saturations are 94% on 28% supplementary oxygen and her respiratory rate is 30/min. A rapid B-type natriuretic peptide (BNP) assay is reported as follows:

BNP	62 pg/ml
-----	----------

What is the best interpretation of this result?

- ☐ A. No conclusion can be drawn from this result
- ☐ B. Pulmonary embolism is the most likely cause of her symptoms
- ☐ C. If a further BNP level is above 50 pg/ml after one hour then this is diagnostic of heart failure
- ☐ D. Heart failure is unlikely to be the cause of her dyspnoea
- ☐ E. Heart failure is highly likely to be the cause of her dyspnoea

[Next question](#)

### B-type natriuretic peptide

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain.

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

#### Effects of BNP

- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

### Clinical uses of BNP

#### Diagnosing patients with acute dyspnoea

- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis
- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure



### Prognosis in patients with chronic heart failure

- initial evidence suggests BNP is an extremely useful marker of prognosis

### Guiding treatment in patients with chronic heart failure

- effective treatment lowers BNP levels

### Screening for cardiac dysfunction

- not currently recommended for population screening

### Question 112 of 247

A 44-year-old man is seen in the cardiology clinic. For the past 6 months he has been experiencing episodes of palpitations associated with pre-syncope symptoms. An ECG taken in clinic shows T wave inversion in leads V1-3 associated with a notch at the end of the QRS complex. He is known to have a family history of sudden cardiac death. What is the most likely diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Arrhythmogenic right ventricular cardiomyopathy       |
| <input type="radio"/> | B. Catecholaminergic polymorphic ventricular tachycardia |
| <input type="radio"/> | C. Hypertrophic obstructive cardiomyopathy               |
| <input type="radio"/> | D. Long QT syndrome                                      |
| <input type="radio"/> | E. Brugada syndrome                                      |

[Next question](#)

The notch at the end of the QRS complex is referred to as an epsilon wave.

#### Arrhythmogenic right ventricular cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a form of inherited cardiovascular disease which may present with syncope or sudden cardiac death. It is generally regarded as the second most common cause of sudden cardiac death in the young after hypertrophic cardiomyopathy.

#### Pathophysiology

- inherited in an autosomal dominant pattern with variable expression
- the right ventricular myocardium is replaced by fibrofatty tissue

#### Presentation

- palpitations
- syncope
- sudden cardiac death

#### Investigation

- ECG abnormalities in V1-3, typically T wave inversion. An epsilon wave is found in about 50% of those with ARV - this is best described as a terminal notch in the QRS complex
- echo changes are often subtle in the early stages but may show an enlarged, hypokinetic right ventricle with a thin free wall
- magnetic resonance imaging is useful to show fibrofatty tissue

#### Management

- drugs: sotalol is the most widely used antiarrhythmic
- catheter ablation to prevent ventricular tachycardia
- implantable cardioverter-defibrillator

#### Naxos disease

- an autosomal recessive variant of ARVC
- a triad of ARVC, palmoplantar keratosis, and woolly hair

### Question 113 of 247

Which one of the following types of hyperlipidaemia are palmar crease xanthoma most commonly associated with?

<input type="radio"/>	A. Familial combined hyperlipidaemia
<input type="radio"/>	B. Lipoprotein lipase deficiency
<input type="radio"/>	C. Familial hypertriglyceridaemia
<input type="radio"/>	D. Remnant hyperlipidaemia
<input type="radio"/>	E. Familial hypercholesterolaemia

[Next question](#)

Palmar crease xanthoma are most strongly associated with remnant hyperlipidaemia

#### Hyperlipidaemia: xanthomata

Characteristic xanthomata seen in hyperlipidaemia:

Palmar xanthoma

- remnant hyperlipidaemia
- may less commonly be seen in familial hypercholesterolaemia

Eruptive xanthoma are due to high triglyceride levels and present as multiple red/yellow vesicles on the extensor surfaces (e.g. elbows, knees)

Causes of eruptive xanthoma

- familial hypertriglyceridaemia
- lipoprotein lipase deficiency

Tendon xanthoma, tuberous xanthoma, xanthelasma

- familial hypercholesterolaemia
- remnant hyperlipidaemia

Xanthelasma are also seen without lipid abnormalities

Management of xanthelasma, options include:

- surgical excision
- topical trichloroacetic acid
- laser therapy
- electrodesiccation

Which one of the following is least associated with ST depression on ECG?

<input type="radio"/>	A. Myocardial ischaemia
<input type="radio"/>	B. Syndrome X
<input type="radio"/>	C. Acute pericarditis
<input type="radio"/>	D. Hypokalaemia
<input type="radio"/>	E. Digoxin

Next question

### ECG: ST depression

Causes of ST depression

- secondary to abnormal QRS (LVH, LBBB, RBBB)
- ischaemia
- digoxin
- hypokalaemia
- syndrome X

Which one of the following is the strongest risk factor for developing infective endocarditis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Previous episode of infective endocarditis |
| <input type="radio"/> | B. Intravenous drug use                       |
| <input type="radio"/> | C. Previous rheumatic fever                   |
| <input type="radio"/> | D. Permanent central venous access line       |
| <input type="radio"/> | E. Recent dental surgery                      |

Next question

Infective endocarditis - strongest risk factor is previous episode of infective endocarditis

### Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. The following types of patients are affected:

- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

### Causes

- *Streptococcus viridans* (most common cause - 40-50%)
- *Staphylococcus epidermidis* (especially prosthetic valves)
- *Staphylococcus aureus* (especially acute presentation, IVDUs)
- *Streptococcus bovis* is associated with colorectal cancer
- non-infective: systemic lupus erythematosus (Libman-Sacks), malignancy: marantic endocarditis

### Culture negative causes

- prior antibiotic therapy
- *Coxiella burnetii*
- *Bartonella*
- *Brucella*
- HACEK: *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, *Kingella*)

Following prosthetic valve surgery *Staphylococcus epidermidis* is the most common organism in the first 2 months and is usually the result of perioperative contamination. After 2 months the spectrum of organisms which cause endocarditis return to normal, except with a slight increase in *Staph. aureus* infections

A 71-year-old man who had a bioprosthetic aortic valve replacement three years ago is reviewed. What antithrombotic therapy is he likely to be taking?

- ☐ A. Nothing
- ☐ B. Aspirin
- ☐ C. Warfarin: INR 2.0-3.0
- ☐ D. Aspirin + clopidogrel
- ☐ E. Warfarin: INR 3.0-4.0

[Next question](#)

#### Prosthetic heart valves - antithrombotic therapy:

- bioprosthetic: aspirin
- mechanical: warfarin + aspirin

### Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	Mechanical valves
Usually bovine or porcine in origin	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays
Major disadvantage is structural deterioration and calcification over time. Most older patients (> 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve	Mechanical valves have a low failure rate
Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication.
	Target INR <ul style="list-style-type: none"> <li>• aortic: 2.0-3.0</li> <li>• mitral: 2.5-3.5</li> </ul>

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.

Which one of the following conditions is most associated with aortic dissection?

<input type="radio"/>	A. Acromegaly
<input type="radio"/>	B. Actinomycosis
<input type="radio"/>	C. Sarcoidosis
<input checked="" type="radio"/>	D. Bicuspid aortic valve
<input type="radio"/>	E. Adult polycystic kidney disease

A bicuspid aortic valve increases the risk of aortic dissection six-fold

### Aortic dissection

Stanford classification

- type A - ascending aorta, 2/3 of cases
- type B - descending aorta, distal to left subclavian origin, 1/3 of cases

DeBakey classification

- type I - originates in ascending aorta, propagates to at least the aortic arch and possibly beyond it distally
- type II - originates in and is confined to the ascending aorta
- type III - originates in descending aorta, rarely extends proximally but will extend distally

Associations

- hypertension
- trauma
- bicuspid aortic valve
- collagens: Marfan's syndrome, Ehlers-Danlos syndrome
- Turner's and Noonan's syndrome
- pregnancy
- syphilis

Complications of backward tear

- aortic incompetence/regurgitation
- MI: inferior pattern often seen due to right coronary involvement

Complications of forward tear

- unequal arm pulses and BP
- stroke
- renal failure



Which of the following congenital heart defects is associated with a bicuspid aortic valve

<input type="radio"/>	A. Tetralogy of Fallot
<input type="radio"/>	B. Ventricular septal defect
<input type="radio"/>	C. Atrial septal defect
<input checked="" type="radio"/>	D. Coarctation of the aorta
<input type="radio"/>	E. Transposition of the great arteries

Next question

## Bicuspid aortic valve

### Overview

- occurs in 1-2% of the population
- usually asymptomatic in childhood
- the majority eventually develop aortic stenosis or regurgitation
- associated with a left dominant coronary circulation (the posterior descending artery arises from the circumflex instead of the right coronary artery) and Turner's syndrome
- around 5% of patients also have coarctation of the aorta

### Complications

- aortic stenosis/regurgitation as above
- higher risk for aortic dissection and aneurysm formation of the ascending aorta

Which of the following conditions is not associated with the development of aortic regurgitation?

<input type="radio"/>	A. Rheumatic fever
<input type="radio"/>	B. Ankylosing spondylitis
<input type="radio"/>	C. Marfan's syndrome
<input type="radio"/>	D. Syphilis
<input type="radio"/>	E. Dilated cardiomyopathy

Next question

Dilated cardiomyopathy is associated with the development of mitral regurgitation, not aortic regurgitation

### Aortic regurgitation

#### Features

- early diastolic murmur
- collapsing pulse
- wide pulse pressure
- mid-diastolic Austin-Flint murmur in severe AR - due to partial closure of the anterior mitral valve cusps caused by the regurgitation streams

#### Causes (due to valve disease)

- rheumatic fever
- infective endocarditis
- connective tissue diseases e.g. RA/SLE
- bicuspid aortic valve

#### Causes (due to aortic root disease)

- aortic dissection
- spondylarthropathies (e.g. ankylosing spondylitis)
- hypertension
- syphilis
- Marfan's, Ehler-Danlos syndrome

A 67-year-old man with a history of chronic obstructive pulmonary disease and ischaemic heart disease is taken to the Emergency Department with dyspnoea. On examination his respiratory rate is 24 / min, JVP is not elevated and crackles are heard in both lung bases. Which other finding would most strongly indicate that his dyspnoea is secondary to isolated left ventricular failure?

<input type="radio"/>	A. Pulsus alternans
<input type="radio"/>	B. Gallop rhythm
<input type="radio"/>	C. Tachycardia
<input type="radio"/>	D. Peripheral oedema
<input type="radio"/>	E. Cardiomegaly on chest x-ray

Gallop rhythm (S3) is an early sign of LVF

Whilst all of the above features may be seen in patients with left ventricular failure a gallop rhythm is one of the most specific and early signs

### Heart sounds

The first heart sound (S1) is caused by closure of the mitral and tricuspid valves whilst the second heart sound (S2) is due to aortic and pulmonary valve closure

#### S1

- closure of mitral and tricuspid valves
- soft if long PR or mitral regurgitation
- loud in mitral stenosis

#### S2

- closure of aortic and pulmonary valves
- soft in aortic stenosis
- splitting during inspiration is normal

#### S3

- caused by diastolic filling of the ventricle
- considered normal if < 30 years old (may persist in women up to 50 years old)
- heard in left ventricular failure (e.g. dilated cardiomyopathy), constrictive pericarditis (called a pericardial knock)

## S4

- may be heard in aortic stenosis, HOCM, hypertension
- caused by atrial contraction against a stiff ventricle
- in HOCM a double apical impulse may be felt as a result of a palpable S4

Next

### Question 121 of 247

A 47-year-old man is admitted to hospital following an acute coronary syndrome. He has a history peptic ulcer disease and his cardiologist decides to use clopidogrel. What is the mechanism of action of clopidogrel?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Non-selective phosphodiesterase inhibitor     |
| <input type="radio"/> | B. Phosphodiesterase V inhibitor                 |
| <input type="radio"/> | C. Inhibits ATP binding to its platelet receptor |
| <input type="radio"/> | D. Inhibits ADP binding to its platelet receptor |
| <input type="radio"/> | E. Glycoprotein IIb/IIIa inhibitor               |

Next question

Clopidogrel inhibits ADP binding to platelet receptors

### Clopidogrel

Clopidogrel is an antiplatelet agent used in the management of cardiovascular disease. It was previously used when aspirin was not tolerated or contraindicated but there are now a number of conditions for which clopidogrel is used in addition to aspirin, for example in patients with an acute coronary syndrome. Following the 2010 NICE technology appraisal clopidogrel is also now first-line in patients following an ischaemic stroke and in patients with peripheral arterial disease.

#### Mechanism

- inhibits ADP binding to its platelet receptor

#### Interactions

- concurrent use of proton pump inhibitors (PPIs) may make clopidogrel less effective (MHRA July 2009)
- this advice was updated by the MHRA in April 2010, evidence seems inconsistent but omeprazole and esomeprazole still cause for concern. Other PPIs such as lansoprazole should be OK - please see the link for more details

Next

### Question 122 of 247

A 72-year-old man presents to the Emergency Department with a broad complex tachycardia. Which of the following features would make it more likely that this was due to a supraventricular tachycardia rather than a ventricular tachycardia?

<input type="radio"/>	A. History of ischaemic heart disease
<input type="radio"/>	B. Left axis deviation
<input type="radio"/>	C. Capture beats
<input type="radio"/>	D. Absence of QRS concordance in chest leads
<input type="radio"/>	E. QRS complex greater than 160 ms

[Next question](#)

Positive QRS concordance in the chest leads is associated with ventricular tachycardia

### Broad complex tachycardia

Features suggesting VT rather than SVT with aberrant conduction

- AV dissociation
- fusion or capture beats
- positive QRS concordance in chest leads
- marked left axis deviation
- history of IHD
- lack of response to adenosine or carotid sinus massage
- QRS > 160 ms

A 66-year-old man presents with shortness-of-breath on exertion. On examination his blood pressure is 128/76 mmHg, pulse 78 / min and regular. Auscultation of his chest reveals an early diastolic murmur. Which one of the following conditions is most associated with this kind of murmur?

<input type="radio"/>	A. Atrial septal defect
<input type="radio"/>	B. Mitral stenosis
<input type="radio"/>	C. Hypertrophic obstructive cardiomyopathy
<input type="radio"/>	D. Aortic regurgitation
<input type="radio"/>	E. Mitral regurgitation

[Next question](#)

## Murmurs

### Ejection systolic

- aortic stenosis
- pulmonary stenosis, HOCM
- ASD, Fallot's

### Pan-systolic

- mitral regurgitation
- tricuspid regurgitation
- VSD

### Late systolic

- mitral valve prolapse
- coarctation of aorta

### Early diastolic

- aortic regurgitation
- Graham-Steel murmur (pulmonary regurgitation)

### Mid diastolic

- mitral stenosis
- Austin-Flint murmur (severe aortic regurgitation)

A 76-year-old woman is admitted with palpitations. During the cardiovascular examination you notice irregular cannon 'a' waves. Which one of the following would account for this finding?

<input type="radio"/>	A. Atrio-ventricular nodal re-entry tachycardia
<input type="radio"/>	B. Atrial fibrillation with tricuspid stenosis
<input type="radio"/>	C. Ventricular tachycardia with 1:1 ventricular-atrial conduction
<input type="radio"/>	D. Complete heart block
<input type="radio"/>	E. Tricuspid regurgitation

[Next question](#)

### JVP: cannon waves

Caused by the right atrium contracting against a closed tricuspid valve. May be subdivided into regular or intermittent

Regular cannon waves

- ventricular tachycardia (with 1:1 ventricular-atrial conduction)
- atrio-ventricular nodal re-entry tachycardia (AVNRT)

Irregular cannon waves

- complete heart block



A 57-year-old man presents to the Emergency Department with a 15 minute history of severe central chest pain radiating to his left arm. ECG shows T-wave inversion in leads I, V5 and V6. Which coronary artery is most likely to be affected?

- ☐ A. Left circumflex
- ☐ B. Posterior interventricular
- ☐ C. Left main stem
- ☐ D. Right coronary
- ☐ E. Left anterior descending

Next question

This is most typical of a left circumflex occlusion although may rarely be seen if the left anterior descending is affected

### ECG: coronary territories

The table below shows the correlation between ECG changes and coronary territories:

	ECG changes	Coronary artery
<b>Anteroseptal</b>	V1-V4	Left anterior descending
<b>Inferior</b>	II, III, aVF	Right coronary
<b>Anterolateral</b>	V4-6, I, aVL	Left anterior descending or left circumflex
<b>Lateral</b>	I, aVL +/- V5-6	Left circumflex
<b>Posterior</b>	Tall R waves V1-2	Usually left circumflex, also right coronary

A 62-year-old female with a history of mitral regurgitation attends her dentist, who intends to perform dental polishing. She is known to be penicillin allergic. What prophylaxis against infective endocarditis should be given?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Oral doxycycline                 |
| <input type="radio"/> | B. Oral erythromycin                |
| <input type="radio"/> | C. No antibiotic prophylaxis needed |
| <input type="radio"/> | D. Oral ofloxacin                   |
| <input type="radio"/> | E. Oral clindamycin                 |

Next question

The 2008 NICE guidelines have fundamentally changed the approach to infective endocarditis prophylaxis. What is not yet clear is if there are any circumstances in which NICE would recommend using antibiotic prophylaxis

### Infective endocarditis: prophylaxis

The 2008 guidelines from NICE have radically changed the list of procedures for which antibiotic prophylaxis is recommended

NICE recommends the following procedures do not require prophylaxis:

- dental procedures
- upper and lower gastrointestinal tract procedures
- genitourinary tract; this includes urological, gynaecological and obstetric procedures and childbirth
- upper and lower respiratory tract; this includes ear, nose and throat procedures and bronchoscopy

The guidelines do however suggest:

- any episodes of infection in people at risk of infective endocarditis should be investigated and treated promptly to reduce the risk of endocarditis developing
- if a person at risk of infective endocarditis is receiving antimicrobial therapy because they are undergoing a gastrointestinal or genitourinary procedure at a site where there is a suspected infection they should be given an antibiotic that covers organisms that cause infective endocarditis

What is the most common cardiac defect seen in Marfan's syndrome

<input type="radio"/>	A. Mitral valve prolapse
<input type="radio"/>	B. Coarctation of the aorta
<input type="radio"/>	C. Bicuspid aortic valve
<input type="radio"/>	D. Dilation of the aortic sinuses
<input type="radio"/>	E. Ventricular septal defect

Next question

Whilst mitral valve prolapse is seen in Marfan's syndrome, dilation of the aortic sinuses is more common

### Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 people.

#### Features

- tall stature with arm span to height ratio  $> 1.05$
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of  $> 20$  degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.

A 72-year-old man who has a history of ischaemic heart disease and left ventricular dysfunction is admitted with dyspnoea. He has not taken his diuretics for three days as he ran out. On examination you note bilateral crackles to the midzones and a respiratory rate of 30/min. Which other clinical finding is most specific with this presentation?

- |                                  |                            |
|----------------------------------|----------------------------|
| <input type="radio"/>            | A. Bisferiens pulse        |
| <input type="radio"/>            | B. Wide pulse pressure     |
| <input type="radio"/>            | C. Warm peripheries        |
| <input checked="" type="radio"/> | D. Pulsus alternans        |
| <input type="radio"/>            | E. Fourth heart sound (S4) |

Pulsus alternans - seen in left ventricular failure

### Pulses

#### Pulsus paradoxus

- greater than the normal (10 mmHg) fall in systolic blood pressure during inspiration --> faint or absent pulse in inspiration
- severe asthma, cardiac tamponade

#### Slow-rising/plateau

- aortic stenosis

#### Collapsing

- aortic regurgitation
- patent ductus arteriosus
- hyperkinetic (anaemia, thyrotoxic, fever, exercise/pregnancy)

#### Pulsus alternans

- regular alternation of the force of the arterial pulse
- severe LVF

#### Bisferiens pulse

- 'double pulse' - two systolic peaks
- mixed aortic valve disease

#### 'Jerky' pulse

- hypertrophic obstructive cardiomyopathy\*

\*HOCM may occasionally be associated with a bisferiens pulse

Next

### Question 129 of 247

A 64-year-old man is admitted to the Emergency Department with chest pain radiating through to his back. On examination pulse 90 regular, BP 140/90. A CXR shows mediastinal widening. A CT shows dissection of the descending aorta. What is the most suitable initial management?

<input type="radio"/>	A. Observe only
<input type="radio"/>	B. IV labetalol
<input type="radio"/>	C. IV sodium nitroprusside
<input type="radio"/>	D. Immediate surgical referral
<input type="radio"/>	E. Oral verapamil

#### Aortic dissection

- type A - ascending aorta - control BP(IV labetalol) + surgery
- type B - descending aorta - control BP(IV labetalol)

Dissection of the descending aorta indicates a type B dissection, which should be managed medically with IV labetalol

#### Aortic dissection: management

##### Stanford classification

- type A - ascending aorta, 2/3 of cases
- type B - descending aorta, distal to left subclavian origin, 1/3 of cases

##### DeBakey classification

- type I - originates in ascending aorta, propagates to at least the aortic arch and possibly beyond it distally
- type II - originates in and is confined to the ascending aorta
- type III - originates in descending aorta, rarely extends proximally but will extend distally

##### Type A

- surgical management, but blood pressure should be controlled to a target systolic of 100-120 mmHg whilst awaiting intervention

## Type B\*

- conservative management
- bed rest
- reduce blood pressure IV labetalol to prevent progression

\*endovascular repair of type B aortic dissection may have a role in the future

Next

### Question 130 of 247

A 52-year-old man is admitted to the Emergency Department. He was found collapsed by neighbours. An ECG on arrival shows torsades de pointes. Which one of his medications is most likely to have contributed to this presentation?

<input type="radio"/>	A. Bisoprolol
<input type="radio"/>	B. Cimetidine
<input type="radio"/>	C. Risperidone
<input type="radio"/>	D. Phenytoin
<input type="radio"/>	E. Doxycycline

### Torsades de pointes

Torsades de pointes ('twisting of the points') is a rare arrhythmia associated with a long QT interval. It may deteriorate into ventricular fibrillation and hence lead to sudden death

#### Causes of long QT interval

- congenital: Jervell-Lange-Nielsen syndrome, Romano-Ward syndrome
- antiarrhythmics: amiodarone, sotalol, class 1a antiarrhythmic drugs
- tricyclic antidepressants
- antipsychotics
- chloroquine
- terfenadine
- erythromycin
- electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia
- myocarditis
- hypothermia
- subarachnoid haemorrhage

#### Management

- IV magnesium sulphate



### Question 131 of 247

Each one of the following is associated with left axis deviation on ECG, except:

<input type="radio"/>	A. Left anterior hemiblock
<input type="radio"/>	B. Ostium primum ASD
<input type="radio"/>	C. Left posterior hemiblock
<input type="radio"/>	D. Obesity
<input type="radio"/>	E. Left bundle branch block

[Next question](#)

### ECG: axis deviation

Causes of left axis deviation (LAD)

- left anterior hemiblock
- left bundle branch block
- Wolff-Parkinson-White syndrome\* - right-sided accessory pathway
- hyperkalaemia
- congenital: ostium primum ASD, tricuspid atresia
- minor LAD in obese people

Causes of right axis deviation (RAD)

- right ventricular hypertrophy
- left posterior hemiblock
- chronic lung disease
- pulmonary embolism
- ostium secundum ASD
- Wolff-Parkinson-White syndrome\* - left-sided accessory pathway
- normal in infant < 1 years old
- minor RAD in tall people

\*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

NICE have produced guidelines on the management of non-ST elevation myocardial infarction (NSTEMI) in which they recommend an approach to treatment based on risk assessment. What cut-off do they recommend for the use of coronary angiography within 96 hours in patients with a NSTEMI?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. All patients with a 12 month mortality risk of greater than 5%  |
| <input type="radio"/> | B. All patients with a 6 month mortality risk of greater than 5%   |
| <input type="radio"/> | C. All patients with a 12 month mortality risk of greater than 10% |
| <input type="radio"/> | D. All patients with a 6 month mortality risk of greater than 1.5% |
| <input type="radio"/> | E. All patients with a 6 month mortality risk of greater than 3%   |

[Next question](#)

NICE NSTEMI/unstable angina guidelines are based on 6 month mortality risk:

- if > 1.5% clopidogrel for 12 months
- if > 3% angiography within 96 hours

### Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive

- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

**Antithrombin** treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is > 265  $\mu\text{mol/l}$  unfractionated heparin should be given.

**Clopidogrel** 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

**Coronary angiography** should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

<b>Aspirin</b>	Antiplatelet - inhibits the production of thromboxane A2
<b>Clopidogrel</b>	Antiplatelet - inhibits ADP binding to its platelet receptor
<b>Enoxaparin</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Fondaparinux</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Bivalirudin</b>	Reversible direct thrombin inhibitor

### Question 133 of 247

Which one of the following is least associated with prolongation of the PR interval?

<input type="radio"/>	A. Digoxin toxicity
<input type="radio"/>	B. Hypocalcaemia
<input type="radio"/>	C. Lyme disease
<input type="radio"/>	D. Rheumatic fever
<input type="radio"/>	E. Ischaemic heart disease

Hypocalcaemia is associated with a prolonged QT interval. Hypokalaemia is associated with a prolonged PR interval

#### ECG: PR interval

Causes of a prolonged PR interval

- idiopathic
- ischaemic heart disease
- digoxin toxicity
- hypokalaemia\*
- rheumatic fever
- aortic root pathology e.g. abscess secondary to endocarditis
- Lyme disease
- sarcoidosis
- myotonic dystrophy

A prolonged PR interval may also be seen in athletes

\*hyperkalaemia can rarely cause a prolonged PR interval, but this is a much less common association than hypokalaemia

### Question 134 of 247

A 64-year-old man who is known to have ischaemic heart disease is due to start a chemotherapy regime which includes doxorubicin. His cardiologist wants to accurately assess his left ventricular function as he is concerned the doxorubicin may damage his myocardium. Which one of the following is the most accurate method to determine his left ventricular function?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. Cardiac computed tomography |
| <input type="radio"/> | B. Echocardiography            |
| <input type="radio"/> | C. Exercise ECG                |
| <input type="radio"/> | D. MUGA scan                   |
| <input type="radio"/> | E. Coronary angiography        |

[Next question](#)

### Cardiac imaging: non-invasive techniques excluding echocardiography

The ability to image the heart using non-invasive techniques such as MRI, CT and radionuclides has evolved rapidly over recent years.

#### Nuclear imaging

These techniques use radiotracers which are extracted by normal myocardium. Examples include:

- thallium
- technetium (99mTc) sestamibi: a coordination complex of the radioisotope technetium-99m with the ligand methoxyisobutyl isonitrile (MIBI), used in 'MIBI' or cardiac Single Photon Emission Computed Tomography (SPECT) scans
- fluorodeoxyglucose (FDG): used in Positron Emission Tomography (PET) scans

The primary role of SPECT is to assess myocardial perfusion and myocardial viability. Two sets of images are usually acquired. First the myocardium at rest followed by images of the myocardium during stress (either exercise or following adenosine / dipyridamole). By comparing the rest with stress images any areas of ischaemia can be classified as reversible or fixed (e.g. Following a myocardial infarction). Cardiac PET is predominately a research tool at the current time

#### MUGA

- Multi Gated Acquisition Scan, also known as radionuclide angiography
- radionuclide (technetium-99m) is injected intravenously
- the patient is placed under a gamma camera
- may be performed as a stress test

- can accurately measure left ventricular ejection fraction. Typically used before and after cardiotoxic drugs are used

## **Cardiac Computed Tomography (CT)**

Cardiac CT is useful for assessing suspected ischaemic heart disease, using two main methods:

- calcium score: there is known to be a correlation between the amount of atherosclerotic plaque calcium and the risk of future ischaemic events. Cardiac CT can quantify the amount of calcium producing a 'calcium score'
- contrast enhanced CT: allows visualisation of the coronary artery lumen

If these two techniques are combined cardiac CT has a very high negative predictive value for ischaemic heart disease.

## **Cardiac MRI**

Cardiac MRI (commonly termed CMR) has become the gold standard for providing structural images of the heart. It is particularly useful when assessing congenital heart disease, determining right and left ventricular mass and differentiating forms of cardiomyopathy. Myocardial perfusion can also be assessed following the administration of gadolinium. Currently CMR provides limited data on the extent of coronary artery disease.

Please also see the British Heart Foundation link for an excellent summary.

### Question 135 of 247

Your next patient is a 74-year-old woman who is known to have type 2 diabetes mellitus. Her blood pressure has been borderline for a number of weeks now but you have decided she would benefit from treatment. Her latest blood pressure is 146/88 mmHg, HbA1c is 7.5% and her BMI is 25 kg/m<sup>2</sup>. What is the most appropriate drug to prescribe?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Bisoprolol          |
| <input type="radio"/> | B. Bendroflumethiazide |
| <input type="radio"/> | C. Amlodipine          |
| <input type="radio"/> | D. Ramipril            |
| <input type="radio"/> | E. Orlistat            |

[Next question](#)

Hypertension in diabetics - ACE-inhibitors are first-line regardless of age

### Diabetes mellitus: hypertension management

Hypertension is an added cardiovascular risk factor for diabetics and should therefore be actively looked for and treated. It is also a risk factor for the development of diabetic nephropathy.

#### Selected points

- the blood pressure target for diabetics is 140/80 mmHg. If there is end-organ damage the target is 130/80 mmHg
- ACE inhibitors are first-line\*. Otherwise managed according to standard NICE hypertension guidelines
- avoid the routine use of beta-blockers in uncomplicated hypertension, particularly when given in combination with thiazides, as they may cause insulin resistance, impair insulin secretion and alter the autonomic response to hypoglycaemia

\*increase insulin sensitivity and can therefore theoretically cause hypoglycaemia - rarely clinically relevant

Which of the following features is not associated with patent ductus arteriosus?

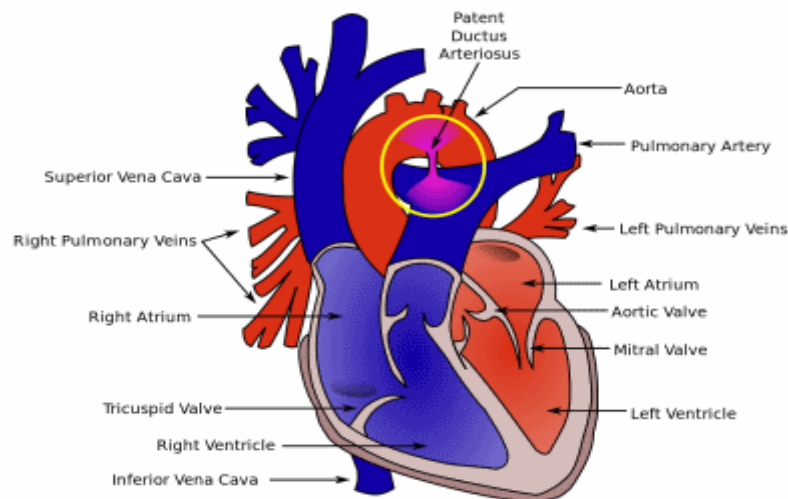
- ☐ A. Continuous 'machinery' murmur
- ☐ B. Bisferiens pulse
- ☐ C. Heaving apex beat
- ☐ D. Wide pulse pressure
- ☐ E. Left subclavicular thrill

PDA is associated with a collapsing pulse

### Patent ductus arteriosus

#### Overview

- acyanotic congenital heart defect
- connection between the pulmonary trunk and descending aorta
- more common in premature babies, born at high altitude or maternal rubella infection in the first trimester



#### Features

- left subclavicular thrill
- continuous 'machinery' murmur
- large volume, bounding, collapsing pulse
- wide pulse pressure
- heaving apex beat

#### Management

- indomethacin closes the connection in the majority of cases
- if associated with another congenital heart defect amenable to surgery then prostaglandin E1 is useful to keep the duct open until after surgical repair



### Question 137 of 247

A 78-year-old woman with no past medical history of note is admitted with palpitations and shortness of breath, having been unwell for the past three days. Examination reveals an irregularly irregular pulse of 130 bpm, a third heart sound, blood pressure of 108/70 mmHg, oxygen saturations of 96% on air and bibasal lung crepitations. What is the most appropriate therapy to control her heart rate?

- ☐ A. Amiodarone
- ☐ B. Flecainide
- ☐ C. Verapamil
- ☐ D. Digoxin
- ☐ E. Bisoprolol

Digoxin is strongly indicated for coexistent atrial fibrillation and heart failure. Beta-blockers should not be introduced until any heart failure has been stabilised. Giving amiodarone or flecainide may result in cardioversion before the patient has been adequately anticoagulated

If there was a more acute history and the patient was in significant heart failure then DC cardioversion would be appropriate, as per Advanced Life Support guidelines

#### Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
Older than 65 years History of ischaemic heart disease	Younger than 65 years Symptomatic First presentation Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) Congestive heart failure

**Question 138 of 247**

Next

A 57-year-old man with NYHA class III heart failure is currently treated with furosemide and ramipril. What is the most suitable beta-blocker to add to improve his long-term prognosis?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Acebutolol |
| <input type="radio"/> | B. Labetalol  |
| <input type="radio"/> | C. Bisoprolol |
| <input type="radio"/> | D. Sotalol    |
| <input type="radio"/> | E. Esmolol    |

Next question

Both carvedilol and bisoprolol have been shown to reduce mortality in stable heart failure. The other beta-blockers have no evidence base to support their use

**Heart failure: drug management**

A number of drugs have been shown to improve mortality in patients with chronic heart failure:

- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide. NICE issued updated guidelines on management in 2010, key points include:

- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate
- if symptoms persist cardiac resynchronisation therapy or digoxin\* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off\*\* pneumococcal vaccine

\*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

\*\*adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years

Next

### Question 139 of 247

Which one of the following is least associated with aortic regurgitation?

<input type="radio"/>	A. Rheumatic fever
<input type="radio"/>	B. William's syndrome
<input type="radio"/>	C. Syphilis
<input type="radio"/>	D. Bicuspid aortic valve
<input type="radio"/>	E. Post-rheumatic disease

[Next question](#)

William's syndrome is associated with supraaortic stenosis.

### Aortic regurgitation

#### Features

- early diastolic murmur
- collapsing pulse
- wide pulse pressure
- mid-diastolic Austin-Flint murmur in severe AR - due to partial closure of the anterior mitral valve cusps caused by the regurgitation streams

#### Causes (due to valve disease)

- rheumatic fever
- infective endocarditis
- connective tissue diseases e.g. RA/SLE
- bicuspid aortic valve

#### Causes (due to aortic root disease)

- aortic dissection
- spondylarthropathies (e.g. ankylosing spondylitis)
- hypertension
- syphilis
- Marfan's, Ehler-Danlos syndrome

A 71-year-old man who is known to have atrial fibrillation comes for review. He had a transient ischaemic attack two weeks ago and takes bendroflumethiazide for hypertension but is otherwise well. His latest blood pressure is 124/76 mmHg. You are discussing management options to try and reduce his future risk of having a stroke. What is his CHA<sub>2</sub>DS<sub>2</sub>-VASc score?

- ☐ A. 1
- ☐ B. 2
- ☐ C. 3
- ☒ D. 4
- ☐ E. 5

[Next question](#)

One point for hypertension, one point for being over the age of 65 years (but under the age of 75 years) and two points ('S2') for the recent TIA.

### Atrial fibrillation: anticoagulation

The European Society of Cardiology published updated guidelines on the management of atrial fibrillation in 2012. They suggest using the **CHA<sub>2</sub>DS<sub>2</sub>-VASc** score to determine the most appropriate anticoagulation strategy. This scoring system superseded the CHADS<sub>2</sub> score.

	Condition	Points
<b>C</b>	Congestive heart failure	1
<b>H</b>	Hypertension (or treated hypertension)	1
<b>A<sub>2</sub></b>	Age $\geq$ 75 years	2
<b>D</b>	Diabetes	1
<b>S<sub>2</sub></b>	Prior Stroke or TIA	2
<b>V</b>	Vascular disease (including ischaemic heart disease and peripheral arterial disease)	1
<b>A</b>	Age 65-74 years	1
<b>S</b>	Sex (female)	1

The table below shows a suggested anticoagulation strategy\* based on the score:

Score	Anticoagulation
0	No treatment is preferred to aspirin
1	Oral anticoagulants preferred to aspirin; dabigatran is an alternative
2 or more	Oral anticoagulants; dabigatran is an alternative

\*the wording in the guidelines ('is preferred to') can be slightly confusing. It basically means that, say for a score of 0, whilst aspirin is an acceptable management option the weight of the clinical evidence would support no treatment instead

A 64-year-old female presents with central chest pain radiating down her left arm of 20 minutes duration. On examination the pulse is 90 bpm and regular and the BP is 205/110 mmHg. ECG shows 2 mm ST elevation in leads V2-6. Morphine and aspirin have already been given. What is the most appropriate next step?

<input type="radio"/>	A. Observe
<input type="radio"/>	B. IV streptokinase
<input type="radio"/>	C. IV alteplase
<input type="radio"/>	D. IV GTN
<input type="radio"/>	E. Temporary pacing

[Next question](#)

The elevated blood pressure would be a contraindication to giving thrombolysis in this patient

### Thrombolysis

Thrombolytic drugs activate plasminogen to form plasmin. This in turn degrades fibrin and help breaks up thrombi. They are primarily used in patients who present with a ST elevation myocardial infarction. Other indications include acute ischaemic stroke and pulmonary embolism, although strict inclusion criteria apply.

#### Examples

- alteplase
- tenecteplase
- streptokinase

#### Contraindications to thrombolysis

- active internal bleeding
- recent haemorrhage, trauma or surgery (including dental extraction)
- coagulation and bleeding disorders
- intracranial neoplasm
- stroke < 3 months
- aortic dissection
- recent head injury
- pregnancy
- severe hypertension

#### Side-effects

- haemorrhage
- hypotension - more common with streptokinase
- allergic reactions may occur with streptokinase

A 65-year-old man is admitted to the Emergency Department with chest pain, nausea and feeling lethargic. He has a history of type 1 diabetes mellitus and is known to have chronic kidney disease stage 4 secondary to diabetic nephropathy. An ECG taken on admission shows widespread ST elevation. Bloods tests show the following:

Na <sup>+</sup>	140 mmol/l
K <sup>+</sup>	5.8 mmol/l
Urea	26 mmol/l
Creatinine	305 µmol/l

His renal function one month ago was as follows:

Na <sup>+</sup>	142 mmol/l
K <sup>+</sup>	4.9 mmol/l
Urea	7.9 mmol/l
Creatinine	199 µmol/l

An echocardiogram shows a small effusion. What is the most appropriate next step in management?

- ☐ A. Oral colchicine
- ☐ B. Pericardiectomy
- ☐ C. Pericardiocentesis
- ☐ D. Intravenous corticosteroids
- ☐ E. Haemodialysis

This patient has uraemic pericarditis. Haemodialysis is urgently required to correct the uraemia which in turn will improve the symptoms of pericarditis.

### Pericarditis

Pericarditis is one of the differentials of any patient presenting with chest pain.

#### Features

- chest pain: may be pleuritic. Is often relieved by sitting forwards
- other symptoms include non-productive cough, dyspnoea and flu-like symptoms
- pericardial rub
- tachypnoea
- tachycardia

#### Causes

- viral infections (Coxsackie)
- tuberculosis
- uraemia (causes 'fibrinous' pericarditis)
- trauma

- post-myocardial infarction, Dressler's syndrome
- connective tissue disease
- hypothyroidism

#### ECG changes

- widespread 'saddle-shaped' ST elevation
- PR depression

### Question 143 of 247

A 62-year-old man is reviewed two hours after a successful elective DC cardioversion for atrial fibrillation. Six weeks ago he presented in fast atrial fibrillation. A decision was made at the time to warfarinise him for six weeks after which he was to be cardioverted. During this time he had a normal transthoracic echocardiogram. He has no past medical history of note other than treatment for a basal cell carcinoma. What is the most appropriate plan regarding anticoagulation?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Can stop immediately                                      |
| <input type="radio"/> | B. Continue warfarinisation for 1 week then review following |
| <input type="radio"/> | C. Lifelong warfarin   |
| <input type="radio"/> | D. Lifelong aspirin  |
| <input type="radio"/> | E. Continue warfarinisation for 4 weeks then review          |

### Atrial fibrillation: cardioversion

#### Onset < 48 hours

If the atrial fibrillation (AF) is definitely of less than 48 hours onset patients should be heparinised. Patients who have risk factors for ischaemic stroke should be put on lifelong oral anticoagulation. Otherwise, patients may be cardioverted using either:

- electrical - 'DC cardioversion'
- pharmacology - amiodarone if structural heart disease, flecainide in those without structural heart disease

Following electrical cardioversion if AF is confirmed as being less than 48 hours duration then further anticoagulation is unnecessary

#### Onset > 48 hours

If the patient has been in AF for more than 48 hours then anticoagulation should be given for at least 3 weeks prior to cardioversion. An alternative strategy is to perform a transoesophageal echo (TOE) to exclude a left atrial appendage (LAA) thrombus. If excluded patients may be heparinised and cardioverted immediately.

If there is a high risk of cardioversion failure (e.g. Previous failure or AF recurrence) then it is recommend to have at least 4 weeks amiodarone or sotalol prior to electrical cardioversion

Following electrical cardioversion patients should be anticoagulated for at least 4 weeks. After this time decisions about anticoagulation should be taken on an individual basis depending on the risk of recurrence



**Question 144 of 247**

Which one of the following is an example of a centrally acting antihypertensive?

<input type="radio"/>	A. Minoxidil
<input type="radio"/>	B. Hydralazine
<input type="radio"/>	C. Sodium nitroprusside
<input type="radio"/>	D. Moxonidine
<input type="radio"/>	E. Diazoxide

[Next question](#)

**Centrally acting antihypertensives**

Examples of centrally acting antihypertensives include:

- methyldopa: used in the management of hypertension during pregnancy
- moxonidine: used in the management of essential hypertension when conventional antihypertensives have failed to control blood pressure
- clonidine: the antihypertensive effect is mediated through stimulating alpha-2 adrenoceptors in the vasomotor centre

A 28-year-old female with a history of primary amenorrhoea and short stature is reviewed in clinic. On examination blood pressure in her right arm is 175/84 mmHg and 170/82 mmHg in her left. What is the most likely cause for her elevated blood pressure?

<input type="radio"/>	A. Coarctation of the aorta
<input type="radio"/>	B. Conn's syndrome
<input type="radio"/>	C. Essential hypertension
<input type="radio"/>	D. Renal aplasia
<input type="radio"/>	E. Renal artery stenosis

[Next question](#)

This patient has Turner's syndrome which is associated with coarctation of the aorta. The site of the coarctation, for example if it involves the origin of the left subclavian artery, determines whether there is a difference between the right and left arm blood pressure readings. There is no significant difference in this case.

Another cause worth considering in a young hypertensive patient with primary amenorrhoea would be congenital adrenal hyperplasia

Essential hypertension would be unusual in a 28-year-old

### Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

#### Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

Eight months after having a prosthetic heart valve a patient develops infective endocarditis. What is the most likely causative organism?

<input type="radio"/>	A. <i>Streptococcus viridans</i>
<input type="radio"/>	B. <i>Staphylococcus aureus</i>
<input type="radio"/>	C. <i>Staphylococcus epidermidis</i>
<input type="radio"/>	D. <i>Coxiella burnetii</i>
<input type="radio"/>	E. One of the HACEK group

Most common cause of endocarditis:

- *Streptococcus viridans*
- *Staphylococcus epidermidis* if < 2 months post valve surgery

*Staphylococcus epidermidis* is the most common causative organism in the first two months following surgery. After this time the spectrum of organisms causing endocarditis returns to normal, with *Streptococcus viridans* being the most common organism

### Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. The following types of patients are affected:

- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

### Causes

- *Streptococcus viridans* (most common cause - 40-50%)
- *Staphylococcus epidermidis* (especially prosthetic valves)
- *Staphylococcus aureus* (especially acute presentation, IVDUs)
- *Streptococcus bovis* is associated with colorectal cancer
- non-infective: systemic lupus erythematosus (Libman-Sacks), malignancy: marantic endocarditis

### Culture negative causes

- prior antibiotic therapy
- *Coxiella burnetii*
- *Bartonella*

- *Brucella*
- HACEK: *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, *Kingella*)

Following prosthetic valve surgery *Staphylococcus epidermidis* is the most common organism in the first 2 months and is usually the result of perioperative contamination. After 2 months the spectrum of organisms which cause endocarditis return to normal, except with a slight increase in *Staph. aureus* infections

### Question 147 of 247

Which one of the following is not a recognised treatment in primary pulmonary hypertension?

<input type="radio"/>	A. Endothelin-1 receptor agonists
<input type="radio"/>	B. Heart-lung transplant
<input type="radio"/>	C. IV prostaglandins
<input type="radio"/>	D. Diuretics
<input type="radio"/>	E. Calcium channel blockers

Endothelin-1 receptor antagonists such as bosentan, not agonists may be used

### Primary pulmonary hypertension

The classification of pulmonary hypertension is currently changing with the term idiopathic pulmonary arterial hypertension (IPAH) becoming more widely used

Primary pulmonary hypertension (PPH, now IPAH)

- pulmonary arterial pressure > 25 mmHg at rest, > 30mmHg with exercise
- PPH is diagnosed when no underlying cause can be found
- around 10% of cases are familial: autosomal dominant
- endothelin thought to play a key role in pathogenesis
- associated with HIV, cocaine and anorexigens (e.g. fenfluramine)

### Features

- more common in females, typically presents at 20-40 years old
- progressive SOB
- cyanosis
- right ventricular heave, loud P2, raised JVP with prominent 'a' waves, tricuspid regurgitation

### Investigation

- echocardiography

### Management

- diuretics if right heart failure
- anticoagulation
- vasodilator therapy: calcium channel blocker, IV prostaglandins, bosentan: endothelin-1 receptor antagonist
- heart-lung transplant

### Question 148 of 247

Which part of the jugular venous waveform is associated with the fall in atrial pressure during ventricular systole?

<input type="radio"/>	A. y descent
<input type="radio"/>	B. v wave
<input type="radio"/>	C. x descent
<input type="radio"/>	D. c wave
<input type="radio"/>	E. a wave

JVP: x descent = fall in atrial pressure during ventricular systole

#### Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis.

'a' wave = atrial contraction

- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves

- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave

- closure of tricuspid valve
- not normally visible

'v' wave

- due to passive filling of blood into the atrium against a closed tricuspid valve
- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve

### Question 149 of 247

Each one of the following may cause left bundle branch block, except:

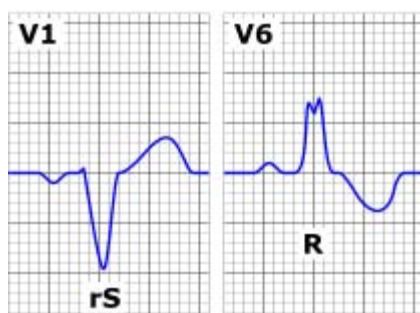
<input type="radio"/>	A. Cardiomyopathy
<input type="radio"/>	B. Atrial septal defect
<input type="radio"/>	C. Hypertension
<input type="radio"/>	D. Idiopathic fibrosis
<input type="radio"/>	E. Ischaemic heart disease

[Next question](#)

Atrial septal defects, both primum and secundum, are associated with right rather than left bundle branch block

### ECG: left bundle branch block

The diagram below shows the typical features of left bundle branch block (LBBB):



One of the most common ways to remember the difference between LBBB and RBBB is WiLLiaM MaRRoW

- in LBBB there is a 'W' in V1 and a 'M' in V6
- in RBBB there is a 'M' in V1 and a 'W' in V6

### Causes of LBBB

- ischaemic heart disease
- hypertension
- aortic stenosis
- cardiomyopathy
- idiopathic fibrosis

A 37-year-old woman presents for review. She is 26 weeks pregnant and has had no problems with her pregnancy to date. Blood pressure is 144/92 mmHg, a rise from her booking reading of 110/80 mmHg. Urine dipstick reveals the following:

Protein	negative
Leucocytes	negative
Blood	negative

What is the most appropriate description of her condition?

- ☐ A. Moderate pre-eclampsia
- ☐ B. Mild pre-eclampsia
- ☐ C. Gestational hypertension
- ☐ D. Normal physiological change in blood pressure
- ☐ E. Pre-existing hypertension

Next question

### Hypertension in pregnancy

The classification of hypertension in pregnancy is complicated and varies. Remember, in normal pregnancy:

- blood pressure usually falls in the first trimester (particularly the diastolic), and continues to fall until 20-24 weeks
- after this time the blood pressure usually increases to pre-pregnancy levels by term

Hypertension in pregnancy is usually defined as:

- systolic > 140 mmHg or diastolic > 90 mmHg
- or an increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic

After establishing that the patient is hypertensive they should be categorised into one of the following groups

Pre-existing hypertension	Pregnancy-induced hypertension (PIH, also known as gestational hypertension)	Pre-eclampsia
<p>A history of hypertension before pregnancy or an elevated blood pressure &gt; 140/90 mmHg before 20 weeks gestation</p> <p>No proteinuria, no oedema</p> <p>Occurs in 3-5% of pregnancies and is more common in older women</p>	<p>Hypertension (as defined above) occurring in the second half of pregnancy (i.e. after 20 weeks)</p> <p>No proteinuria, no oedema</p> <p>Occurs in around 5-7% of pregnancies</p> <p>Resolves following birth (typically after one month). Women with PIH are at increased risk of future pre-eclampsia or hypertension later in life</p>	<p>Pregnancy-induced hypertension in association with proteinuria (&gt; 0.3g / 24 hours)</p> <p>Oedema may occur but is now less commonly used as a criteria</p> <p>Occurs in around 5% of pregnancies</p>



**Question 151 of 247**

Next

A 68-year-old man with a past history of aortic stenosis is reviewed in clinic. Which one of the following features would most guide the timing of surgery?

<input type="radio"/>	A. Symptomatology of patient
<input type="radio"/>	B. Aortic valve gradient of 50 mmHg
<input type="radio"/>	C. Pulse pressure
<input type="radio"/>	D. Loudness of murmur
<input type="radio"/>	E. Left ventricular ejection fraction

Aortic stenosis management: AVR if symptomatic, otherwise cut-off is gradient of 50 mmHg

**Aortic stenosis**

Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis

- degenerative calcification (most common cause in older patients > 65 years)
- bicuspid aortic valve (most common cause in younger patients < 65 years)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management

- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Which of the following conditions is least associated with coarctation of the aorta?

<input type="radio"/>	A. Neurofibromatosis
<input type="radio"/>	B. Bicuspid aortic valve
<input type="radio"/>	C. Prader-Willi syndrome
<input type="radio"/>	D. Turner's syndrome
<input type="radio"/>	E. Berry aneurysms

Next question

### Coarctation of the aorta

Coarctation of the aorta describes a congenital narrowing of the descending aorta.

#### Overview

- more common in males (despite association with Turner's syndrome)

#### Features

- infancy: heart failure
- adult: hypertension
- radio-femoral delay
- mid systolic murmur, maximal over back
- apical click from the aortic valve
- notching of the inferior border of the ribs (due to collateral vessels) is not seen in young children

#### Associations

- Turner's syndrome
- bicuspid aortic valve
- berry aneurysms
- neurofibromatosis

Which one of the following statements regarding prosthetic heart valves is correct?

- ☐ A. Antibiotic prophylaxis is still recommended for patients with mechanical valves who have dental procedures
- ☐ B. The majority of mechanical valves are of the ball-and-cage type
- ☐ C. Bioprosthetic valves are now usually obtained from human cadavers
- ☐ D. The target INR for patients with mechanical aortic valves is 3.0-4.0
- ☐ E. Mechanical valves have a lower failure rate than bioprosthetic valves

Next question

### Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	Mechanical valves
Usually bovine or porcine in origin	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays
Major disadvantage is structural deterioration and calcification over time. Most older patients ( > 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve	Mechanical valves have a low failure rate
Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication.
	Target INR <ul style="list-style-type: none"> <li>• aortic: 2.0-3.0</li> <li>• mitral: 2.5-3.5</li> </ul>

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.

Which one of the following statements regarding percutaneous coronary intervention (PCI) is incorrect?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Stent thrombosis usually occurs in the first month                                  |
| <input type="radio"/> | B. Restenosis is more common than stent thrombosis                                     |
| <input type="radio"/> | C. Around 95% of patients have a stent fitted during a PCI                             |
| <input type="radio"/> | D. Renal impairment is a risk factor for restenosis                                    |
| <input type="radio"/> | E. Patients with drug-eluting stents require a shorter duration of clopidogrel therapy |

Next question

PCI - patients with drug-eluting stents require a longer duration of clopidogrel therapy

### Percutaneous coronary intervention

Percutaneous coronary intervention (PCI) is a technique used to restore myocardial perfusion in patients with ischaemic heart disease, both in patients with stable angina and acute coronary syndromes. Stents are implanted in around 95% of patients - it is now rare for just balloon angioplasty to be performed

Following stent insertion migration and proliferation of smooth muscle cells and fibroblasts occur to the treated segment. The stent struts eventually become covered by endothelium. Until this happens there is an increased risk of platelet aggregation leading to thrombosis.

Two main complications may occur

- stent thrombosis: due to platelet aggregation as above. Occurs in 1-2% of patients, most commonly in the first month. Usually presents with acute myocardial infarction
- restenosis: due to excessive tissue proliferation around stent. Occurs in around 5-20% of patients, most commonly in the first 3-6 months. Usually presents with the recurrence of angina symptoms. Risk factors include diabetes, renal impairment and stents in venous bypass grafts

Types of stent

- bare-metal stent (BMS)
- drug-eluting stents (DES): stent coated with paclitaxel or rapamycin which inhibit local tissue growth. Whilst this reduces restenosis rates the stent thrombosis rates are increased as the process of stent endothelialisation is slowed

Following insertion the most important factor in preventing stent thrombosis is antiplatelet therapy. Aspirin should be continued indefinitely. The length of clopidogrel treatment depends on the type of stent, reason for insertion and consultant preference

You review a 75-year-old man who complains of palpitations. He was diagnosed with atrial fibrillation around four months ago and started on digoxin 125 mcg od and warfarin. Despite this treatment he still feels his 'heart race' regularly. On examination his pulse is 96 / min irregularly irregular and respiratory examination is unremarkable. What is the most appropriate next step in management?

- ☐ A. Switch digoxin for verapamil
- ☐ B. Refer for electrical cardioversion
- ☐ C. Add amiodarone
- ☐ D. Add bisoprolol
- ☐ E. Make no change to his regular medication but prescribe flecainide as a 'pill in the pocket'

Adding a beta-blocker would be the best option here. It will help control the heart rate and may have cardioprotective properties in certain patients (e.g. Those with heart failure, ischaemic heart disease or hypertension).

#### Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
Older than 65 years History of ischaemic heart disease	Younger than 65 years Symptomatic First presentation Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) Congestive heart failure

A 34-year-old man is investigated following an unexplained collapse whilst at work. A resting ECG shows convex ST elevation in V1-V3 with a partial right bundle branch block pattern. What is the most likely diagnosis?

<input type="radio"/>	A. Catecholaminergic polymorphic ventricular tachycardia
<input type="radio"/>	B. Hypertrophic obstructive cardiomyopathy
<input type="radio"/>	C. Arrhythmogenic right ventricular cardiomyopathy
<input type="radio"/>	D. Brugada syndrome
<input type="radio"/>	E. Normal variant

[Next question](#)

### Brugada syndrome

Brugada syndrome is a form of inherited cardiovascular disease which may present with sudden cardiac death. It is inherited in an autosomal dominant fashion and has an estimated prevalence of 1:5,000-10,000. Brugada syndrome is more common in Asians.

#### Pathophysiology

- a large number of variants exist
- around 20-40% of cases are caused by a mutation in the SCN5A gene which encodes the myocardial sodium ion channel protein

#### ECG changes

- convex ST elevation V1-V3
- partial right bundle branch block
- changes may be more apparent following flecainide

#### Management

- implantable cardioverter-defibrillator

A 74-year-old man is admitted with chest pain associated with ECG changes. A troponin T taken 12 hours after admission indicates an acute myocardial infarction. Which one of the following is most likely to predict a poor prognosis?

- ☐ A. History of diabetes mellitus
- ☐ B. Loss of heart rate variability
- ☐ C. Left ventricular ejection fraction of 40%
- ☐ D. Diastolic blood pressure of 110 mmHg
- ☐ E. Male sex

Next question

### Acute coronary syndrome: prognostic factors

The 2006 Global Registry of Acute Coronary Events (GRACE) study has been used to derive regression models to predict death in hospital and death after discharge in patients with acute coronary syndrome

Poor prognostic factors

- age
- development (or history) of heart failure
- peripheral vascular disease
- reduced systolic blood pressure
- Killip class\*
- initial serum creatinine concentration
- elevated initial cardiac markers
- cardiac arrest on admission
- ST segment deviation

\***Killip class** - system used to stratify risk post myocardial infarction

Killip class	Features	30 day mortality
I	No clinical signs heart failure	6%
II	Lung crackles, S3	17%
III	Frank pulmonary oedema	38%
IV	Cardiogenic shock	81%

A 62-year-old patient presents to the Emergency Department with a 25 minute history of crushing central chest pain. ECG shows ST elevation in leads I and aVL. Which coronary territory is likely to be affected?

- ☐ A. Lateral
- ☐ B. Posterior
- ☐ C. Anteroseptal
- ☐ D. Anterolateral
- ☐ E. Inferior

[Next question](#)

These ECG changes are most consistent with a lateral myocardial infarction. An anterolateral infarction is more likely to have changes in the chest leads.

### ECG: coronary territories

The table below shows the correlation between ECG changes and coronary territories:

	ECG changes	Coronary artery
<b>Anteroseptal</b>	V1-V4	Left anterior descending
<b>Inferior</b>	II, III, aVF	Right coronary
<b>Anterolateral</b>	V4-6, I, aVL	Left anterior descending or left circumflex
<b>Lateral</b>	I, aVL +/- V5-6	Left circumflex
<b>Posterior</b>	Tall R waves V1-2	Usually left circumflex, also right coronary



A 64-year-old man with a history of ischaemic heart disease and poor left ventricular function presents with a broad complex tachycardia of 140 bpm. On examination blood pressure is 110/74 mmHg. Fusion and capture beats are seen on the 12 lead ECG. What is the first line drug management?

<input type="radio"/>	A. Sotalol
<input type="radio"/>	B. Amiodarone
<input type="radio"/>	C. Adenosine
<input type="radio"/>	D. Flecainide
<input type="radio"/>	E. Lidocaine

[Next question](#)

The history of ischaemic heart disease combined with the presence of fusion and capture beats strongly suggests a diagnosis of ventricular tachycardia (VT). Whilst lidocaine can also be used in VT, amiodarone would be preferred given his history of poor left ventricular function. In the 2010 joint European Resuscitation Council and Resuscitation Council (UK) guidelines amiodarone is also considered first-line in a peri-arrest situation

### Ventricular tachycardia: management

Whilst a broad complex tachycardia may result from a supraventricular rhythm with aberrant conduction, the European Resuscitation Council advise that in a peri-arrest situation it is assumed to be ventricular in origin

If the patient has adverse signs (systolic BP < 90 mmHg, chest pain, heart failure or rate > 150 beats/min) then immediate cardioversion is indicated. In the absence of such signs antiarrhythmics may be used. If these fail, then electrical cardioversion may be needed with synchronised DC shocks

#### Drug therapy

- amiodarone: ideally administered through a central line
- lidocaine: use with caution in severe left ventricular impairment
- procainamide

Verapamil should NOT be used in VT

#### If drug therapy fails

- electrophysiological study (EPS)
- implantable cardioverter-defibrillator (ICD) - this is particularly indicated in patients with significantly impaired LV function

You have ordered a B-type natriuretic peptide (BNP) test on a patient with suspected heart failure. It has come back as being slightly elevated. Which one of the following factors may account for a falsely elevated BNP?

- ☐ A. ACE inhibitor therapy
- ☐ B. Beta-blocker therapy
- ☐ C. Furosemide therapy
- ☐ D. Obesity
- ☐ E. COPD

### Heart failure: diagnosis

NICE issued updated guidelines on diagnosis and management in 2010. The choice of investigation is determined by whether the patient has previously had a myocardial infarction or not.

Previous myocardial infarction

- arrange echocardiogram within 2 weeks

No previous myocardial infarction

- measure serum natriuretic peptides (BNP)
- if levels are 'high' arrange echocardiogram within 2 weeks
- if levels are 'raised' arrange echocardiogram within 6 weeks

### Serum natriuretic peptides

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain. Very high levels are associated with a poor prognosis.

	BNP	NTproBNP
<b>High levels</b>	> 400 pg/ml (116 pmol/litre)	> 2000 pg/ml (236 pmol/litre)
<b>Raised levels</b>	100-400 pg/ml (29-116 pmol/litre)	400-2000 pg/ml (47-236 pmol/litre)
<b>Normal levels</b>	< 100 pg/ml (29 pmol/litre)	< 400 pg/ml (47 pmol/litre)

Factors which alter the BNP level:

Increase BNP levels	Decrease BNP levels
Left ventricular hypertrophy Ischaemia Tachycardia Right ventricular overload Hypoxaemia (including pulmonary embolism) GFR < 60 ml/min Sepsis COPD Diabetes Age > 70 Liver cirrhosis	Obesity Diuretics ACE inhibitors Beta-blockers Angiotensin 2 receptor blockers Aldosterone antagonists

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Next

A 52-year-old female is referred from the Emergency Department with a pulse of 36 beats/min. The ECG shows complete heart block with a narrow QRS complex. Blood pressure is 88/50 mmHg and there is no evidence of heart failure. What is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Transvenous pacing                            |
| <input type="radio"/> | B. Transcutaneous pacing                         |
| <input type="radio"/> | C. Isoprenaline infusion, titrated to heart rate |
| <input type="radio"/> | D. No intervention but cardiac monitoring        |
| <input type="radio"/> | E. Intravenous atropine                          |

**Peri-arrest rhythms: bradycardia**

The 2010 Resuscitation Council (UK) guidelines emphasise that the management of bradycardia depends on:

- 1. identifying the presence of signs indicating haemodynamic compromise - 'adverse signs'
- 2. identifying the potential risk of asystole

**Adverse signs**

The following factors indicate haemodynamic compromise and hence the need for treatment:

- shock: hypotension (systolic blood pressure < 90 mmHg), pallor, sweating,

cold, clammy extremities, confusion or impaired consciousness

- syncope
- myocardial ischaemia
- heart failure

Atropine is the first line treatment in this situation. If this fails to work, or there is the potential risk of asystole then transvenous pacing is indicated

**Potential risk of asystole**

The following indicate a potential risk of asystole and hence the need for treatment with transvenous pacing:

- complete heart block with broad complex QRS
- recent asystole
- Mobitz type II AV block
- ventricular pause > 3 seconds

If there is a delay in the provision of transvenous pacing the following interventions may be used:

- atropine, up to maximum of 3mg
- transcutaneous pacing
- adrenaline infusion titrated to response

A 60-year-old man is admitted with severe central chest pain to the resus department. The admission ECG shows ST elevation in leads V1-V4 with reciprocal changes in the inferior leads. Which one of the following is most likely to account for these findings?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. 75% occlusion of the left anterior descending artery  |
| <input type="radio"/> | B. 75% occlusion of the left circumflex artery           |
| <input type="radio"/> | C. 75% occlusion of the right coronary artery            |
| <input type="radio"/> | D. 100% occlusion of the left circumflex artery          |
| <input type="radio"/> | E. 100% occlusion of the left anterior descending artery |

Next question

Widespread ST elevation in this territory implies a complete occlusion of the left anterior descending artery.

### ECG: ST elevation

#### Causes of ST elevation

- myocardial infarction
- pericarditis
- normal variant - 'high take-off'
- left ventricular aneurysm
- Prinzmetal's angina (coronary artery spasm)
- rare: subarachnoid haemorrhage, part of spectrum of changes in hyperkalaemia

Next

### Question 163 of 247

A 70-year-old man is admitted to the Acute Medicine Unit as he is pyrexial and feeling generally unwell. He has a history of ischaemic heart disease and had a myocardial infarction 5 years ago. An echocardiogram is arranged which shows a small vegetation around the mitral valve. Blood cultures are taken which are reported as follows:

*Streptococcus viridans*

What is the most appropriate antibiotic therapy?

- ☐ A. IV benzylpenicillin
- ☐ B. IV benzylpenicillin + ceftriaxone
- ☐ C. IV flucloxacillin + gentamicin
- ☐ D. IV vancomycin + rifampicin + gentamicin
- ☐ E. IV vancomycin + benzylpenicillin

[Next question](#)

### Infective endocarditis: prognosis and management

Poor prognostic factors

- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism

- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)

Scenario	Suggested antibiotic therapy
Initial blind therapy	Flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
Initial blind therapy if prosthetic valve is present or patient is penicillin allergic	Vancomycin + rifampicin + gentamicin
Endocarditis caused by staphylococci	Flucloxacillin (add rifampicin if prosthetic valve, vancomycin + rifampicin if penicillin allergic or MRSA)

Native valve endocarditis caused by fully-sensitive streptococci (e.g. viridans)	Benzylpenicillin (large vegetation, intracardial abscess or infected emboli then benzylpenicillin + gentamicin, vancomycin if penicillin allergic)
Native valve endocarditis caused by less sensitive streptococci OR prosthetic valve endocarditis caused by streptococci	Benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

#### Indications for surgery

- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

Next

### Question 164 of 247

A 54-year-old man with atypical chest pain is referred to cardiology. An exercise ECG shows non-specific ST and T wave changes. Following this an coronary angiogram is performed which demonstrates no evidence of atherosclerosis. A diagnosis of Prinzmetal's angina is suspected. What is the most appropriate first-line treatment?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Nicorandil             |
| <input type="radio"/> | B. Atenolol               |
| <input type="radio"/> | C. Felodipine             |
| <input type="radio"/> | D. Fluoxetine             |
| <input type="radio"/> | E. Isosorbide mononitrate |

Prinzmetal angina - treatment = dihydropyridine calcium channel blocker

See the SIGN guidelines for more details.

### Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery. NICE produced guidelines in 2011 covering the management of stable angina

#### Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- NICE recommend using either a beta-blocker or a calcium channel blocker first-line based on 'comorbidities, contraindications and the person's preference'
- if a calcium channel blocker is used as monotherapy a rate-limiting one such as verapamil or diltiazem should be used. If used in combination with a beta-blocker then use a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine). Remember that beta-blockers should not be prescribed concurrently with verapamil (risk of complete heart block)
- if there is a poor response to initial treatment then medication should be increased to the maximum tolerated dose (e.g. for atenolol 100mg od)
- if a patient is still symptomatic after monotherapy with a beta-blocker add a calcium channel blocker and vice versa
- if a patient is on monotherapy and cannot tolerate the addition of a calcium channel blocker or a beta-blocker then consider one of the following drugs: a long-acting nitrate, ivabradine, nicorandil or ranolazine
- if a patient is taking both a beta-blocker and a calcium-channel blocker then only add a third drug whilst a patient is awaiting assessment for PCI or CABG

#### Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy

- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

#### Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the  $I_f$  ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina



### Question 165 of 247

A 76-year-old man is reviewed. He was recently admitted after being found to be in atrial fibrillation. This was his second episode of atrial fibrillation. He also takes ramipril for hypertension but has no other history of note. During admission he was warfarinised and discharged with planned follow-up in the cardiology clinic. However, on review today he is found to be in sinus rhythm. What should happen regarding anticoagulation?

- ☐ A. Stop warfarin
- ☐ B. Continue warfarin for 1 month
- ☐ C. Stop warfarin + start aspirin
- ☐ D. Continue lifelong warfarin
- ☐ E. Continue warfarin for 6 months

Warfarin should be continued indefinitely as this is his second episode of atrial fibrillation and he has risk factors for stroke (age, hypertension)

#### Atrial fibrillation: anticoagulation

The European Society of Cardiology published updated guidelines on the management of atrial fibrillation in 2012. They suggest using the **CHA<sub>2</sub>DS<sub>2</sub>-VASc** score to determine the most appropriate anticoagulation strategy. This scoring system superseded the CHADS<sub>2</sub> score.

	Condition	Points
<b>C</b>	Congestive heart failure	1
<b>H</b>	Hypertension (or treated hypertension)	1
<b>A<sub>2</sub></b>	Age $\geq$ 75 years	2
<b>D</b>	Diabetes	1
<b>S<sub>2</sub></b>	Prior Stroke or TIA	2
<b>V</b>	Vascular disease (including ischaemic heart disease and peripheral arterial disease)	1
<b>A</b>	Age 65-74 years	1
<b>S</b>	Sex (female)	1

The table below shows a suggested anticoagulation strategy\* based on the score:

Score	Anticoagulation
0	No treatment is preferred to aspirin
1	Oral anticoagulants preferred to aspirin; dabigatran is an alternative
2 or more	Oral anticoagulants; dabigatran is an alternative

\*the wording in the guidelines ('is preferred to') can be slightly confusing. It basically means that, say for a score of 0, whilst aspirin is an acceptable management option the weight of the clinical evidence would support no treatment instead

Which of the following is responsible for the rapid depolarisation phase of the myocardial action potential?

- ☐ A. Rapid sodium influx
- ☐ B. Slow sodium efflux
- ☐ C. Slow efflux of calcium
- ☐ D. Efflux of potassium
- ☐ E. Rapid calcium influx

[Next question](#)

## Electrical activity of the heart

### Myocardial action potential

Phase	Description	Mechanism
0	Rapid depolarisation	Rapid sodium influx These channels automatically deactivate after a few ms
1	Early repolarisation	Efflux of potassium
2	Plateau	Slow influx of calcium
3	Final repolarisation	Efflux of potassium
4	Restoration of ionic concentrations	Resting potential is restored by $\text{Na}^+/\text{K}^+$ ATPase There is slow entry of $\text{Na}^+$ into the cell decreasing the potential difference until the threshold potential is reached, triggering a new action potential

NB cardiac muscle remains contracted 10-15 times longer than skeletal muscle

### Conduction velocity

Atrial conduction	Spreads along ordinary atrial myocardial fibres at 1 m/sec
AV node conduction	0.05 m/sec
Ventricular conduction	Purkinje fibres are of large diameter and achieve velocities of 2-4 m/sec (this allows a rapid and coordinated contraction of the ventricles)

Which one of the following types of hyperlipidaemia are eruptive xanthoma most commonly associated with?

<input type="radio"/>	A. Familial hypertriglyceridaemia
<input type="radio"/>	B. Familial hypercholesterolaemia
<input type="radio"/>	C. Familial combined hyperlipidaemia
<input type="radio"/>	D. Remnant hyperlipidaemia
<input type="radio"/>	E. Hyperlipidaemia secondary to nephrotic syndrome

Next question

### Hyperlipidaemia: xanthomata

Characteristic xanthomata seen in hyperlipidaemia:

Palmar xanthoma

- remnant hyperlipidaemia
- may less commonly be seen in familial hypercholesterolaemia

Eruptive xanthoma are due to high triglyceride levels and present as multiple red/yellow vesicles on the extensor surfaces (e.g. elbows, knees)

Causes of eruptive xanthoma

- familial hypertriglyceridaemia
- lipoprotein lipase deficiency

Tendon xanthoma, tuberous xanthoma, xanthelasma

- familial hypercholesterolaemia
- remnant hyperlipidaemia

Xanthelasma are also seen without lipid abnormalities

Management of xanthelasma, options include:

- surgical excision
- topical trichloroacetic acid
- laser therapy
- electrodesiccation

Which of the following statements concerning the third heart sound is correct?

<input type="radio"/>	A. Caused by systolic filling of the ventricle
<input type="radio"/>	B. May be heard in constrictive pericarditis
<input type="radio"/>	C. Associated with atrial septal defects
<input type="radio"/>	D. Is characteristically soft in aortic stenosis
<input type="radio"/>	E. Caused by atrial contraction against a stiff ventricle

Next question

A third heart sound is often heard in left ventricular failure and constrictive pericarditis

### Heart sounds

The first heart sound (S1) is caused by closure of the mitral and tricuspid valves whilst the second heart sound (S2) is due to aortic and pulmonary valve closure

#### S1

- closure of mitral and tricuspid valves
- soft if long PR or mitral regurgitation
- loud in mitral stenosis

#### S2

- closure of aortic and pulmonary valves
- soft in aortic stenosis
- splitting during inspiration is normal

#### S3

- caused by diastolic filling of the ventricle
- considered normal if < 30 years old (may persist in women up to 50 years old)
- heard in left ventricular failure (e.g. dilated cardiomyopathy), constrictive pericarditis (called a pericardial knock)

#### S4

- may be heard in aortic stenosis, HOCM, hypertension
- caused by atrial contraction against a stiff ventricle
- in HOCM a double apical impulse may be felt as a result of a palpable S4

A 14-year-old boy is admitted with palpitations and is noted to have a long QT interval. His only past medical history is deafness. What is the likely diagnosis?

- ☐ A. Leriche's syndrome
- ☐ B. Wolff-Parkinson White syndrome
- ☐ C. Jervell-Lange-Nielsen syndrome
- ☐ D. Romano-Ward syndrome
- ☐ E. Osler-Weber-Rendu syndrome

Jervell-Lange-Nielsen syndrome is associated with profound deafness and a prolonged QT interval

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"> <li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li> <li>Romano-Ward syndrome (no deafness)</li> </ul>	<ul style="list-style-type: none"> <li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li> <li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li> <li>methadone</li> <li>chloroquine</li> <li>terfenadine**</li> <li>erythromycin</li> </ul>	<ul style="list-style-type: none"> <li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li> <li>acute myocardial infarction</li> <li>myocarditis</li> <li>hypothermia</li> <li>subarachnoid haemorrhage</li> </ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

### Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

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Which of the following congenital heart defects may progress to Eisenmenger's syndrome?

<input type="radio"/>	A. Tetralogy of Fallot
<input type="radio"/>	B. Coarctation of the aorta
<input type="radio"/>	C. Patent ductus arteriosus
<input type="radio"/>	D. Tricuspid atresia
<input type="radio"/>	E. Transposition of the great arteries

Although patients with tetralogy of Fallot have, by definition, a ventricular septal defect they do not go on to develop Eisenmenger's syndrome

### Eisenmenger's syndrome

Describes the reversal of a left to right shunt in a congenital heart defect due to pulmonary hypertension

Associated with

- VSD
- ASD
- PDA

Features

- original murmur may disappear
- cyanosis
- clubbing
- right ventricular failure
- haemoptysis, embolism

Management

- heart-lung transplantation is required

### Question 171 of 247

What is the normal cross sectional area of the mitral valve?

<input type="radio"/>	A.	1-2 sq cm
<input type="radio"/>	B.	3-4 sq cm
<input type="radio"/>	C.	4-6 sq cm
<input type="radio"/>	D.	6-8 sq cm
<input type="radio"/>	E.	8-10 sq cm

[Next question](#)

### Mitral stenosis

It is said that the causes of mitral stenosis are rheumatic fever, rheumatic fever and rheumatic fever. Rarer causes that may be seen in the MRCP include mucopolysaccharidoses, carcinoid and endocardial fibroelastosis

#### Features

- mid-diastolic murmur (best heard in expiration)
- loud S1, opening snap
- low volume pulse
- malar flush
- atrial fibrillation

#### Features of severe MS

- length of murmur increases
- opening snap becomes closer to S2

#### Echocardiography

- the normal cross sectional area of the mitral valve is 4-6 sq cm. A 'tight' mitral stenosis implies a cross sectional area of < 1 sq cm



The use of beta-blockers in treating hypertension has declined sharply in the past five years. Which one of the following best describes the reasons why this has occurred?

- ☐ A. Less likely to prevent stroke + potential impairment of glucose tolerance
- ☐ B. Less likely to prevent myocardial infarctions + potential impairment of glucose tolerance
- ☐ C. High rate of interactions with other commonly prescribed medications (e.g. Calcium channel blockers)
- ☐ D. Increased incidence of reported adverse effects
- ☐ E. Increased incidence of chronic obstructive pulmonary disease

Next question

This was demonstrated in the Anglo-Scandinavian Cardiac Outcomes Trial-Blood Pressure Lowering Arm (ASCOT-BPLA).

### Hypertension: diagnosis and management

NICE published updated guidelines for the management of hypertension in 2011. Some of the key changes include:

- classifying hypertension into stages
- recommending the use of ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM)
- calcium channel blockers are now considered superior to thiazides
- bendroflumethiazide is no longer the thiazide of choice

### Blood pressure classification

This becomes relevant later in some of the management decisions that NICE advocate.

<b>Stage 1 hypertension</b>	Clinic BP $\geq$ 140/90 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 135/85 mmHg
<b>Stage 2 hypertension</b>	Clinic BP $\geq$ 160/100 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 150/95 mmHg
<b>Severe hypertension</b>	Clinic systolic BP $\geq$ 180 mmHg, or clinic diastolic BP $\geq$ 110 mmHg

### Diagnosing hypertension

If a BP reading is  $\geq$  140 / 90 mmHg patients should be offered ABPM to confirm the diagnosis.

Patients with a BP reading of  $\geq$  180/110 mmHg should be considered for immediate treatment.

Ambulatory blood pressure monitoring (ABPM)

- at least 2 measurements per hour during the person's usual waking hours (for example, between 08:00 and 22:00)
- use the average value of at least 14 measurements

If ABPM is not tolerated or declined HBPM should be offered.

Home blood pressure monitoring (HBPM)

- for each BP recording, two consecutive measurements need to be taken, at least 1 minute apart and with the person seated
- BP should be recorded twice daily, ideally in the morning and evening
- BP should be recorded for at least 4 days, ideally for 7 days
- discard the measurements taken on the first day and use the average value of all the remaining measurements

## Managing hypertension

ABPM/HBPM  $\geq$  135/85 mmHg (i.e. stage 1 hypertension)

- treat if  $< 80$  years of age and any of the following apply; target organ damage, established cardiovascular disease, renal disease, diabetes or a 10-year cardiovascular risk equivalent to 20% or greater

ABPM/HBPM  $\geq$  150/95 mmHg (i.e. stage 2 hypertension)

- offer drug treatment regardless of age

For patients  $< 40$  years consider specialist referral to exclude secondary causes.

Step 1 treatment

- patients  $< 55$ -years-old: ACE inhibitor (A)
- patients  $> 55$ -years-old or of Afro-Caribbean origin: calcium channel blocker

Step 2 treatment

- ACE inhibitor + calcium channel blocker (A + C)

Step 3 treatment

- add a thiazide diuretic (D, i.e. A + C + D)
- NICE now advocate using either chlorthalidone (12.5-25.0 mg once daily) or indapamide (1.5 mg modified-release once daily or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide

NICE define a clinic BP  $\geq 140/90$  mmHg after step 3 treatment with optimal or best tolerated doses as resistant hypertension. They suggest step 4 treatment or seeking expert advice

#### Step 4 treatment

- consider further diuretic treatment
- if potassium  $< 4.5$  mmol/l add spironolactone 25mg od
- if potassium  $> 4.5$  mmol/l add higher-dose thiazide-like diuretic treatment
- if further diuretic therapy is not tolerated, or is contraindicated or ineffective, consider an alpha- or beta-blocker

If BP still not controlled seek specialist advice.

#### Blood pressure targets

	Clinic BP	ABPM / HBPM
Age $< 80$ years	140/90 mmHg	135/85 mmHg
Age $> 80$ years	150/90 mmHg	145/85 mmHg

#### New drugs

##### Direct renin inhibitors

- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

A 29-year-old woman is investigated for increasing dyspnoea and feeling generally weak and lethargic. Over the past few months she has had five episodes of syncope, some of which occurred following exercise. There is no past medical history of note although her grandmother died aged 44 years after suffering increasing shortness-of-breath and syncope. On examination her oxygen saturations are 98% on room air and the pulse is 78 / min. The second heart sound is loud but no murmurs are heard. Auscultation of the chest is unremarkable. What is the most likely diagnosis?

<input type="radio"/>	A. Pulmonary arterial hypertension
<input type="radio"/>	B. Familial pulmonary stenosis
<input type="radio"/>	C. Hypertrophic obstructive cardiomyopathy
<input type="radio"/>	D. Catecholaminergic polymorphic ventricular tachycardia
<input type="radio"/>	E. Arrhythmogenic right ventricular dysplasia

[Next question](#)

### Pulmonary arterial hypertension: features and management

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise.

#### Features

- exertional dyspnoea is the most frequent symptom
- chest pain and syncope may also occur
- loud P2
- left parasternal heave (due to right ventricular hypertrophy)

Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy. Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide

If there is a positive response to acute vasodilator testing

- oral calcium channel blockers

If there is a negative response to acute vasodilator testing

- prostacyclin analogues: treprostinil, iloprost
- endothelin receptor antagonists: bosentan
- phosphodiesterase inhibitors: sildenafil

Each one of the following may cause secondary hypertension, except:

<input type="radio"/>	A. Patent ductus arteriosus
<input type="radio"/>	B. Cushing's syndrome
<input type="radio"/>	C. Liddle's syndrome
<input type="radio"/>	D. 11-beta hydroxylase deficiency
<input type="radio"/>	E. Combined oral contraceptive pill

Next question

### Hypertension: secondary causes

Renal - accounts for 80% of secondary hypertension

- glomerulonephritis
- pyelonephritis
- adult polycystic kidney disease
- renal artery stenosis

Endocrine disorders

- Cushing's syndrome
- primary hyperaldosteronism including Conn's syndrome
- Liddle's syndrome
- congenital adrenal hyperplasia (11-beta hydroxylase deficiency)
- pheochromocytoma
- acromegaly

Others

- pregnancy
- coarctation of the aorta
- the combined oral contraceptive pill
- steroids
- MAOI

A 29-year-old woman who is 28 weeks pregnant is reviewed. She has developed pre-eclampsia with her current blood pressure being 156/104 mmHg and the urine dipstick reported as follows:

Protein	+
Leucocytes	negative
Blood	negative

There is no oedema and the patient is otherwise asymptomatic. Of the following drugs, which one is least suitable to use?

- ☐ A. Labetalol
- ☐ B. Nifedipine
- ☐ C. Losartan
- ☐ D. Methyldopa
- ☐ E. Hydralazine

Next question

ACE inhibitors and angiotensin-2 receptor blockers should be avoided as they are teratogenic. Most clinicians would either use methyldopa or labetalol first-line in this situation

### Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria ( $> 0.3\text{g} / 24 \text{ hours}$ ). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

Risk factors

- $> 40$  years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index  $> 30 \text{ kg/m}^2$
- diabetes mellitus

- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

#### Features of severe pre-eclampsia

- hypertension: typically > 170/110 mmHg and proteinuria as above
- proteinuria: dipstick ++/+++
- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count <  $100 \times 10^6/l$ , abnormal liver enzymes or HELLP syndrome

#### Management

- consensus guidelines recommend treating blood pressure > 160/110 mmHg although many clinicians have a lower threshold
- oral labetalol is now first-line following the 2010 NICE guidelines. Nifedipine and hydralazine may also be used
- delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario

Next

### Question 176 of 247

A 60-year-old man who is investigated for exertional chest pain is diagnosed as having angina pectoris. Which one of the following drugs is most likely to improve his long-term prognosis?

<input type="radio"/>	A. Atenolol
<input type="radio"/>	B. Aspirin
<input type="radio"/>	C. Isosorbide mononitrate
<input type="radio"/>	D. Ramipril
<input type="radio"/>	E. Nicorandil

[Next question](#)

Strong evidence exists supporting the use of aspirin in stable angina. The benefit of ACE inhibitors and beta-blockers are significant in patients who've had a myocardial infarction but modest in those with stable angina. Please see the CKS link for a review of the most recent trials.

### Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery. NICE produced guidelines in 2011 covering the management of stable angina

#### Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- NICE recommend using either a beta-blocker or a calcium channel blocker first-line based on 'comorbidities, contraindications and the person's preference'
- if a calcium channel blocker is used as monotherapy a rate-limiting one such as verapamil or diltiazem should be used. If used in combination with a beta-blocker then use a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine). Remember that beta-blockers should not be prescribed concurrently with verapamil (risk of complete heart block)
- if there is a poor response to initial treatment then medication should be increased to the maximum tolerated dose (e.g. for atenolol 100mg od)
- if a patient is still symptomatic after monotherapy with a beta-blocker add a calcium channel blocker and vice versa
- if a patient is on monotherapy and cannot tolerate the addition of a calcium channel blocker or a beta-blocker then consider one of the following drugs: a long-acting nitrate, ivabradine, nicorandil or ranolazine
- if a patient is taking both a beta-blocker and a calcium-channel blocker then only add a third drug whilst a patient is awaiting assessment for PCI or CABG

#### Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy



- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

#### Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the  $I_f$  ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

Next

### Question 177 of 247

Which one of the following is least associated with Tetralogy of Fallot?

<input type="radio"/>	A. Right ventricular outflow tract obstruction
<input type="radio"/>	B. Overriding aorta
<input type="radio"/>	C. Ejection systolic murmur
<input type="radio"/>	D. Left-to-right shunt
<input type="radio"/>	E. Right ventricular hypertrophy

[Next question](#)

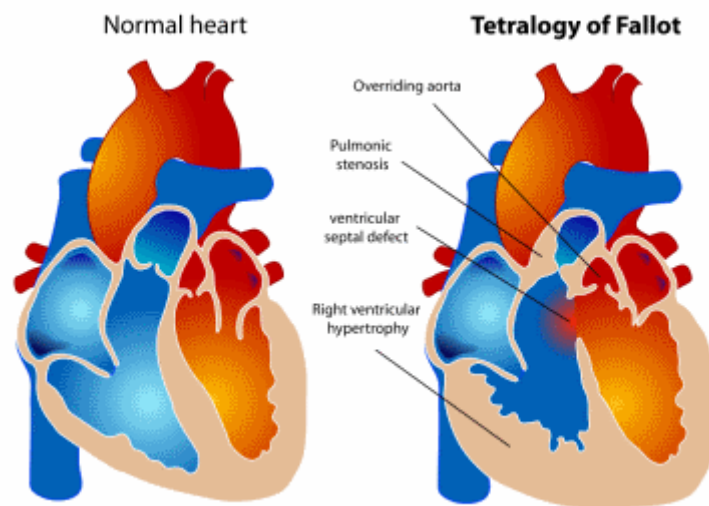
Right-to-left shunting is characteristic of Fallot's. It is however known that a small number of asymptomatic infants may initially have a degree of left-to-right shunting through the ventricular septal defect

### Tetralogy of Fallot

Tetralogy of Fallot (TOF) is the most common cause of cyanotic congenital heart disease\*. It typically presents at around 1-2 months, although may not be picked up until the baby is 6 months old

The four characteristic features are:

- ventricular septal defect (VSD)
- right ventricular hypertrophy
- right ventricular outflow tract obstruction, pulmonary stenosis
- overriding aorta



The severity of the right ventricular outflow tract obstruction determines the degree of cyanosis and clinical

severity

#### Other features

- cyanosis
- causes a right-to-left shunt
- ejection systolic murmur due to pulmonary stenosis (the VSD doesn't usually cause a murmur)
- a right-sided aortic arch is seen in 25% of patients
- chest x-ray shows a 'boot-shaped' heart, ECG shows right ventricular hypertrophy

#### Management

- surgical repair is often undertaken in two parts
- cyanotic episodes may be helped by beta-blockers to reduce infundibular spasm

\*however, at birth transposition of the great arteries is the more common lesion as patients with TOF generally present at around 1-2 months

Next

### Question 178 of 247

Each one of the following is an indication for an implantable cardiac defibrillator, except:

<input type="radio"/>	A. Previous myocardial infarction with non-sustained VT on 24 hr monitoring
<input type="radio"/>	B. Wolff-Parkinson White syndrome
<input type="radio"/>	C. Hypertrophic obstructive cardiomyopathy
<input type="radio"/>	D. Previous cardiac arrest due to VF
<input type="radio"/>	E. Long QT syndrome

[Next question](#)

## Implantable cardiac defibrillators

### Indications

- long QT syndrome
- hypertrophic obstructive cardiomyopathy
- previous cardiac arrest due to VT/VF
- previous myocardial infarction with non-sustained VT on 24 hr monitoring, inducible VT on electrophysiology testing and ejection fraction < 35%
- Brugada syndrome

[Next](#)

### Question 179 of 247

Which one of the following statements regarding catecholaminergic polymorphic ventricular tachycardia (CPVT) is correct?

<input type="radio"/>	A. Resting ECG typically shows T wave inversion in leads V1-V3
<input type="radio"/>	B. Beta-blockers are contraindicated in patients with CPVT
<input type="radio"/>	C. Is associated with cleft palate
<input type="radio"/>	D. In the majority of cases is due to a defect in the potassium channel
<input type="radio"/>	E. Symptoms generally develop before the age of 20 years

[Next question](#)

### Catecholaminergic polymorphic ventricular tachycardia

Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a form of inherited cardiac disease associated with sudden cardiac death. It is inherited in an autosomal dominant fashion and has a prevalence of around 1:10,000.

#### Pathophysiology

- the most common cause is a defect in the ryanodine receptor (RYR2) which is found in the myocardial sarcoplasmic reticulum

#### Features

- exercise or emotion induced polymorphic ventricular tachycardia resulting in syncope
- sudden cardiac death
- symptoms generally develop before the age of 20 years

#### Management

- beta-blockers
- implantable cardioverter-defibrillator

Which one of the following is least associated with Wolff-Parkinson White syndrome?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. Mitral valve prolapse       |
| <input type="radio"/> | B. Ebstein's anomaly           |
| <input type="radio"/> | C. Thyrotoxicosis              |
| <input type="radio"/> | D. Coarctation of the aorta    |
| <input type="radio"/> | E. Hypertrophic cardiomyopathy |

### Wolff-Parkinson White

Wolff-Parkinson White (WPW) syndrome is caused by a congenital accessory conducting pathway between the atria and ventricles leading to a atrioventricular re-entry tachycardia (AVRT). As the accessory pathway does not slow conduction AF can degenerate rapidly to VF

Possible ECG features include:

- short PR interval
- wide QRS complexes with a slurred upstroke - 'delta wave'
- left axis deviation if right-sided accessory pathway\*
- right axis deviation if left-sided accessory pathway\*

Differentiating between type A and type B

- type A (left-sided pathway): dominant R wave in V1
- type B (right-sided pathway): no dominant R wave in V1

Associations of WPW

- HOCM
- mitral valve prolapse
- Ebstein's anomaly
- thyrotoxicosis
- secundum ASD

Management

- definitive treatment: radiofrequency ablation of the accessory pathway
- medical therapy: sotalol\*\*, amiodarone, flecainide

\*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

\*\*sotalol should be avoided if there is coexistent atrial fibrillation as prolonging the refractory period at the AV node may increase the rate of transmission through the accessory pathway, increasing the ventricular rate and potentially deteriorating into ventricular fibrillation

Which one of the following cardiac conditions is most associated with a louder murmur following the Valsalva manoeuvre?

<input type="radio"/>	A. Mitral stenosis
<input type="radio"/>	B. Aortic stenosis
<input type="radio"/>	C. Ventricular septal defect
<input type="radio"/>	D. Hypertrophic obstructive cardiomyopathy
<input type="radio"/>	E. Aortic regurgitation

[Next question](#)

### HOCM: features

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

#### Features

- often asymptomatic
- dyspnoea, angina, syncope
- sudden death (most commonly due to ventricular arrhythmias), arrhythmias, heart failure
- jerky pulse, large 'a' waves, double apex beat
- ejection systolic murmur: increases with Valsalva manoeuvre and decreases on squatting

#### Associations

- Friedreich's ataxia
- Wolff-Parkinson White

#### Echo - mnemonic - MR SAM ASH

- mitral regurgitation (MR)
- systolic anterior motion (SAM) of the anterior mitral valve leaflet
- asymmetric hypertrophy (ASH)

#### ECG

- left ventricular hypertrophy
- progressive T wave inversion
- deep Q waves
- atrial fibrillation may occasionally be seen

You are called to review a 78-year-old man on the surgical wards. He is three days post-op following a colectomy. He was recently diagnosed with colon cancer (Duke's C) and has a history of polymyalgia rheumatica. Current medications include co-codamol 30/500, prednisolone and prophylactic dose low-molecular weight heparin. Five minutes ago he started to complain of severe central chest pain. An ECG performed by the nurses shows ST elevation in the anterior leads. Aspirin and oxygen have been given by the Foundation 1 doctor. What is the most appropriate treatment?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. IV diamorphine + increase low-molecular weight heparin to treatment dose + double his prednisolone dose |
| <input type="radio"/> | B. IV diamorphine + arrange echocardiogram urgently to exclude pericardial tamponade                       |
| <input type="radio"/> | C. IV diamorphine + call the family in to discuss withdrawal of treatment                                  |
| <input type="radio"/> | D. IV diamorphine + arrange percutaneous coronary intervention   |
| <input type="radio"/> | E. IV diamorphine + thrombolysis   |

Primary percutaneous coronary intervention is the most appropriate treatment given his recent operation and associated risk of bleeding.

### Myocardial infarction: management

A number of studies over the past 10 years have provided an evidence for the management of ST-elevation myocardial infarction (STEMI)

In the absence of contraindications, all patients should be given

- aspirin
- clopidogrel: the two major studies (CLARITY and COMMIT) both confirmed benefit but used different loading doses (300mg and 75mg respectively)
- low molecular weight heparin

NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO<sub>2</sub>) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO<sub>2</sub> of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO<sub>2</sub> of 88-92% until blood gas analysis is available.

Primary percutaneous coronary intervention (PCI) has emerged as the gold-standard treatment for STEMI but is not available in all centres. Thrombolysis should be performed in patients without access to primary PCI

With regards to thrombolysis:



- tissue plasminogen activator (tPA) has been shown to offer clear mortality benefits over streptokinase
- tenecteplase is easier to administer and has been shown to have non-inferior efficacy to alteplase with a similar adverse effect profile

An ECG should be performed 90 minutes following thrombolysis to assess whether there has been a greater than 50% resolution in the ST elevation

- if there has not been adequate resolution then rescue PCI is superior to repeat thrombolysis
- for patients successfully treated with thrombolysis PCI has been shown to be beneficial. The optimal timing of this is still under investigation

Next

### Question 183 of 247

You are considering prescribing an antibiotic to a 28-year-old man who tells you he has Long QT syndrome. Which antibiotic is it most important to avoid?

- ☐ A. Doxycycline
- ☐ B. Trimethoprim
- ☐ C. Erythromycin
- ☐ D. Rifampicin
- ☐ E. Co-amoxiclav

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"><li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li><li>Romano-Ward syndrome (no deafness)</li></ul>	<ul style="list-style-type: none"><li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li><li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li><li>methadone</li><li>chloroquine</li><li>terfenadine**</li><li>erythromycin</li></ul>	<ul style="list-style-type: none"><li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li><li>acute myocardial infarction</li><li>myocarditis</li><li>hypothermia</li><li>subarachnoid haemorrhage</li></ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

### Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

Next

### Question 184 of 247

Which part of the ECG complex corresponds with the closure of the mitral valve?

<input type="radio"/>	A. P wave
<input type="radio"/>	B. PR interval
<input type="radio"/>	C. QRS complex
<input type="radio"/>	D. ST segment
<input type="radio"/>	E. T wave

A diagram of the cardiac cycle can be found on the external link

### Heart sounds

The first heart sound (S1) is caused by closure of the mitral and tricuspid valves whilst the second heart sound (S2) is due to aortic and pulmonary valve closure

S1

- closure of mitral and tricuspid valves
- soft if long PR or mitral regurgitation
- loud in mitral stenosis

S2

- closure of aortic and pulmonary valves
- soft in aortic stenosis
- splitting during inspiration is normal

S3

- caused by diastolic filling of the ventricle
- considered normal if < 30 years old (may persist in women up to 50 years old)
- heard in left ventricular failure (e.g. dilated cardiomyopathy), constrictive pericarditis (called a pericardial knock)

S4

- may be heard in aortic stenosis, HOCM, hypertension
- caused by atrial contraction against a stiff ventricle
- in HOCM a double apical impulse may be felt as a result of a palpable S4

### Question 185 of 247

Where is the most common site for primary cardiac tumours to occur in adults?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Left atrium           |
| <input type="radio"/> | B. Right ventricle       |
| <input type="radio"/> | C. Right atrium          |
| <input type="radio"/> | D. Left atrial appendage |
| <input type="radio"/> | E. Left ventricle        |

[Next question](#)

Atrial myxoma - commonest site = left atrium

The most common site of atrial myxomas is at the fossa ovalis border in the left atrium

#### Atrial myxoma

##### Overview

- 75% occur in left atrium
- more common in females

##### Features

- systemic: weight loss, fever, clubbing
- emboli
- atrial fibrillation
- mid-diastolic murmur, 'tumour plop'

[Next](#)

### Question 186 of 247

A 56-year-old man with a past history of ischaemic heart disease is admitted with central chest pain radiating to his left arm associated with nausea. On arrival in the Coronary Care Unit he is noted to be in complete heart block. Which coronary artery is likely to be affected?

<input type="radio"/>	A. Circumflex
<input type="radio"/>	B. Right coronary
<input type="radio"/>	C. Obtuse marginal
<input type="radio"/>	D. Left anterior descending
<input type="radio"/>	E. Posterior descending

[Next question](#)

The right coronary artery supplies the atrioventricular node in 90% of patients

### Coronary circulation

#### Arterial supply of the heart

- left aortic sinus --> left coronary artery (LCA)
- right aortic sinus --> right coronary artery (RCA)
- LCA --> LAD + circumflex
- RCA --> posterior descending
- RCA supplies SA node in 60%, AV node in 90%

#### Venous drainage of the heart

- coronary sinus drains into the right atrium

A 70-year-old man with a background of ischaemic heart disease and peripheral arterial disease presents to the Emergency Department. He has been feeling generally unwell for the past two days with fever and myalgia but this morning developed a purple, cold left middle toe. On examination there are signs of early ischaemia to the toe and a faint livedo reticularis rash is seen on the foot. A diagnosis of cholesterol embolisation is suspected. Which of the following features would be most supportive of this diagnosis?

<input type="radio"/>	A. Lymphocytosis
<input type="radio"/>	B. Thrombocytosis
<input type="radio"/>	C. Neutrophilia
<input type="radio"/>	D. Thrombocytopaenia
<input type="radio"/>	E. Eosinophilia

[Next question](#)

Eosinophilia is seen in around 70% of cases of cholesterol embolisation.

### Cholesterol embolisation

#### Overview

- cholesterol emboli may break off causing renal disease
- seen more commonly in arteriopathies, abdominal aortic aneurysms

#### Features

- eosinophilia
- purpura
- renal failure
- livedo reticularis

A 58-year-old man who is taking lithium for bipolar disorder presents for review. During routine examination he found to be hypertensive with a blood pressure of 166/82 mmHg. This is confirmed with two separate readings. Urine dipstick is negative and renal function is normal. What is the most appropriate medication to start?

<input type="radio"/>	A. Amlodipine
<input type="radio"/>	B. Ramipril
<input type="radio"/>	C. Losartan
<input type="radio"/>	D. Bendroflumethiazide
<input type="radio"/>	E. Doxazosin

[Next question](#)

Diuretics, ACE-inhibitors and angiotensin II receptor antagonists may cause lithium toxicity. The BNF advises that neurotoxicity may be increased when lithium is given with diltiazem or verapamil but there is no significant interaction with amlodipine. Alpha-blockers are not listed as interacting with lithium but they would not be first-line treatment for hypertension.

The NICE hypertension guidelines suggest amlodipine wouldn't be a bad first choice, even if we ignore his lithium treatment.

### Lithium toxicity

Lithium is mood stabilising drug used most commonly prophylactically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys. Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

#### Features of toxicity

- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

#### Management

- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion



Which one of the following features is not part of the modified Duke criteria used in the diagnosis of infective endocarditis?

<input type="radio"/>	A. Prolonged PR interval
<input type="radio"/>	B. Positive serology for <i>Coxiella burnetii</i>
<input type="radio"/>	C. Fever > 38°C
<input type="radio"/>	D. Roth spots
<input type="radio"/>	E. Positive microbiology from embolic fragments

A prolonged PR interval is part of the diagnostic criteria of rheumatic fever. The modified Duke criteria have now been adopted in the latest guidelines from the European Society of Cardiology. Details can be found in the link below

### Infective endocarditis: Modified Duke criteria

Infective endocarditis diagnosed if

- pathological criteria positive, or
- 2 major criteria, or
- 1 major and 3 minor criteria, or
- 5 minor criteria

### Pathological criteria

Positive histology or microbiology of pathological material obtained at autopsy or cardiac surgery (valve tissue, vegetations, embolic fragments or intracardiac abscess content)

### Major criteria

Positive blood cultures

- two positive blood cultures showing typical organisms consistent with infective endocarditis, such as *Streptococcus viridans* and the HACEK group, or
- persistent bacteraemia from two blood cultures taken > 12 hours apart or three or more positive blood cultures where the pathogen is less specific such as *Staph aureus* and *Staph epidermidis*, or
- positive serology for *Coxiella burnetii*, *Bartonella* species or *Chlamydia psittaci*, or
- positive molecular assays for specific gene targets

Evidence of endocardial involvement

- positive echocardiogram (oscillating structures, abscess formation, new valvular regurgitation or dehiscence of prosthetic valves), or
- new valvular regurgitation

### Minor criteria

- predisposing heart condition or intravenous drug use
- microbiological evidence does not meet major criteria

- fever > 38°C
- vascular phenomena: major emboli, splenomegaly, clubbing, splinter haemorrhages, petechiae or purpura
- immunological phenomena: glomerulonephritis, Osler's nodes, Roth spots, Janeway lesions

Next

### Question 190 of 247

A 71-year-old man who had rheumatic fever as a child is admitted to the cardiology ward with suspected infective endocarditis. This is confirmed by blood cultures and echocardiography. Which one of the following is most likely to represent a need for surgical intervention?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. A septic embolism in the right kidney                    |
| <input type="radio"/> | B. Persistent pyrexia after 48 hours of antibiotics         |
| <input type="radio"/> | C. Lengthening of the PR interval on ECG                    |
| <input type="radio"/> | D. Pre-existing left ventricular impairment                 |
| <input type="radio"/> | E. <i>Streptococcus viridans</i> isolated on blood cultures |

[Next question](#)

Infective endocarditis - indications for surgery:

- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

Lengthening of the PR interval is likely to represent an aortic root abscess which will require surgical intervention.

### Infective endocarditis: prognosis and management

Poor prognostic factors

- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism

- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)

Scenario	Suggested antibiotic therapy
Initial blind therapy	Flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
Initial blind therapy if prosthetic valve is present or patient is penicillin allergic	Vancomycin + rifampicin + gentamicin
Endocarditis caused by staphylococci	Flucloxacillin (add rifampicin if prosthetic valve, vancomycin + rifampicin if penicillin allergic or MRSA)
Native valve endocarditis caused by fully-sensitive streptococci (e.g. viridans)	Benzylpenicillin (large vegetation, intracardial abscess or infected emboli then benzylpenicillin + gentamicin, vancomycin if penicillin allergic)
Native valve endocarditis caused by less sensitive streptococci OR prosthetic valve endocarditis caused by streptococci	Benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

### Indications for surgery

- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

Next

### Question 191 of 247

A 61-year-old man is admitted with central crushing chest pain to the Emergency Department. An ECG taken immediately on arrival shows ST-elevation in leads II, III and aVF. His only past medical history of note is hypertension for which he takes ramipril, aspirin and simvastatin. What is the optimum management of this patient?

(LMWH = low-molecular weight heparin)

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Aspirin + clopidogrel + LMWH + repeat ECG in 20 minutes                           |
| <input type="radio"/> | B. Clopidogrel + LMWH + alteplase  |
| <input type="radio"/> | C. Aspirin + clopidogrel + LMWH + tenecteplase                                       |
| <input type="radio"/> | D. Aspirin + clopidogrel + LMWH + alteplase  |
| <input type="radio"/> | E. Aspirin + clopidogrel + IV heparin + immediate percutaneous coronary intervention |

[Next question](#)

Primary percutaneous coronary intervention is the gold-standard treatment for ST-elevation myocardial infarction

### Myocardial infarction: management

A number of studies over the past 10 years have provided an evidence for the management of ST-elevation myocardial infarction (STEMI)

In the absence of contraindications, all patients should be given

- aspirin
- clopidogrel: the two major studies (CLARITY and COMMIT) both confirmed benefit but used different loading doses (300mg and 75mg respectively)
- low molecular weight heparin

NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO<sub>2</sub>) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO<sub>2</sub> of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO<sub>2</sub> of 88-92% until blood gas analysis is available.

Primary percutaneous coronary intervention (PCI) has emerged as the gold-standard treatment for STEMI but is not available in all centres. Thrombolysis should be performed in patients without access to primary PCI

With regards to thrombolysis:

- tissue plasminogen activator (tPA) has been shown to offer clear mortality benefits over streptokinase
- tenecteplase is easier to administer and has been shown to have non-inferior efficacy to alteplase with a similar adverse effect profile

An ECG should be performed 90 minutes following thrombolysis to assess whether there has been a greater than 50% resolution in the ST elevation

- if there has not been adequate resolution then rescue PCI is superior to repeat thrombolysis
- for patients successfully treated with thrombolysis PCI has been shown to be beneficial. The optimal timing of this is still under investigation

Next

### Question 192 of 247

Which one of the following drugs is best avoided in patients with hypertrophic obstructive cardiomyopathy?

<input type="radio"/>	A. Amiodarone
<input type="radio"/>	B. Verapamil
<input type="radio"/>	C. Ramipril
<input type="radio"/>	D. Amoxicillin
<input type="radio"/>	E. Atenolol

[Next question](#)

HOCM - drugs to avoid: nitrates, ACE-inhibitors, inotropes

Verapamil should however be avoided in patients with coexistent Wolff-Parkinson White as it may precipitate VT or VF

### HOCM: management

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. The estimated prevalence is 1 in 500.

#### Management

- Amiodarone
- Beta-blockers or verapamil for symptoms
- Cardioverter defibrillator
- Dual chamber pacemaker
- Endocarditis prophylaxis\*

#### Drugs to avoid

- nitrates
- ACE-inhibitors
- inotropes

\*although see the 2008 NICE guidelines on infective endocarditis prophylaxis

Each one of the following is associated with aortic dissection, except:

<input type="radio"/>	A. Ventricular septal defect
<input type="radio"/>	B. Turner's syndrome
<input type="radio"/>	C. Noonan's syndrome
<input type="radio"/>	D. Pregnancy
<input type="radio"/>	E. Marfan's syndrome

### Aortic dissection

Stanford classification

- type A - ascending aorta, 2/3 of cases
- type B - descending aorta, distal to left subclavian origin, 1/3 of cases

DeBakey classification

- type I - originates in ascending aorta, propagates to at least the aortic arch and possibly beyond it distally
- type II - originates in and is confined to the ascending aorta
- type III - originates in descending aorta, rarely extends proximally but will extend distally

Associations

- hypertension
- trauma
- bicuspid aortic valve
- collagens: Marfan's syndrome, Ehlers-Danlos syndrome
- Turner's and Noonan's syndrome
- pregnancy
- syphilis

Complications of backward tear

- aortic incompetence/regurgitation
- MI: inferior pattern often seen due to right coronary involvement

Complications of forward tear

- unequal arm pulses and BP
- stroke
- renal failure



Which part of the jugular venous waveform is associated with the opening of the tricuspid valve?

<input type="radio"/>	A. x descent
<input type="radio"/>	B. v wave
<input type="radio"/>	C. a wave
<input type="radio"/>	D. c wave
<input type="radio"/>	E. y descent

Next question

JVP: y descent = opening of tricuspid valve

### Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis.

'a' wave = atrial contraction

- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves

- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave

- closure of tricuspid valve
- not normally visible

'v' wave

- due to passive filling of blood into the atrium against a closed tricuspid valve
- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve

A 60-year-old man is investigated for progressive shortness of breath. On examination a loud P2 is noted associated with a left parasternal heave. An ECG shows evidence of right ventricular strain and a diagnosis of pulmonary hypertension is suspected. Which one of the following is the single most important test to confirm the diagnosis?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Echocardiography               |
| <input type="radio"/> | B. High resolution CT thorax      |
| <input type="radio"/> | C. Cardiac catheterisation        |
| <input type="radio"/> | D. Pulmonary angiography          |
| <input type="radio"/> | E. Ventilation perfusion scanning |

[Next question](#)

Whilst echocardiography may strongly point towards a diagnosis of pulmonary hypertension all patients need to have right heart pressures measured. Cardiac catheterisation is therefore the single most important investigation. Please see the British Thoracic Society guidelines for more details.

### Pulmonary arterial hypertension: features and management

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise.

#### Features

- exertional dyspnoea is the most frequent symptom
- chest pain and syncope may also occur
- loud P2
- left parasternal heave (due to right ventricular hypertrophy)

Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy. Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide

If there is a positive response to acute vasodilator testing

- oral calcium channel blockers

If there is a negative response to acute vasodilator testing

- prostacyclin analogues: treprostinil, iloprost
- endothelin receptor antagonists: bosentan
- phosphodiesterase inhibitors: sildenafil

A 49-year-old man with idiopathic pulmonary arterial hypertension has a negative acute vasodilator test. Which one of the following medications is least likely to be beneficial in his long-term management?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Nifedipine   |
| <input type="radio"/> | B. Treprostinil |
| <input type="radio"/> | C. Bosentan     |
| <input type="radio"/> | D. Sildenafil   |
| <input type="radio"/> | E. Warfarin     |

Next question

Oral calcium channel blockers are unlikely to be beneficial following a negative acute vasodilator test

### Pulmonary arterial hypertension: features and management

Pulmonary arterial hypertension (PAH) may be defined as a sustained elevation in mean pulmonary arterial pressure of greater than 25 mmHg at rest or 30 mmHg after exercise.

#### Features

- exertional dyspnoea is the most frequent symptom
- chest pain and syncope may also occur
- loud P2
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Management should first involve treating any underlying conditions, for example with anticoagulants or oxygen. Following this, it has now been shown that **acute vasodilator testing** is central to deciding on the appropriate management strategy. Acute vasodilator testing aims to decide which patients show a significant fall in pulmonary arterial pressure following the administration of vasodilators such as intravenous epoprostenol or inhaled nitric oxide

If there is a positive response to acute vasodilator testing

- oral calcium channel blockers

If there is a negative response to acute vasodilator testing

- prostacyclin analogues: treprostinil, iloprost
- endothelin receptor antagonists: bosentan
- phosphodiesterase inhibitors: sildenafil

Which of the following is least associated with primary pulmonary hypertension?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. HIV                          |
| <input type="radio"/> | B. Fenfluramine                 |
| <input type="radio"/> | C. Recurrent pulmonary embolism |
| <input type="radio"/> | D. Loud P2                      |
| <input type="radio"/> | E. Right ventricular heave      |

Recurrent pulmonary embolism is a cause of secondary pulmonary hypertension

Some candidates have questioned whether HIV, cocaine and fenfluramine should be regarded as secondary causes of pulmonary hypertension. This is a fair point and the situation should be improved with the new classification of pulmonary hypertension. However, faced with this question in the exam the correct answer would be recurrent pulmonary embolism - a classical cause of secondary pulmonary hypertension

### Primary pulmonary hypertension

The classification of pulmonary hypertension is currently changing with the term idiopathic pulmonary arterial hypertension (IPAH) becoming more widely used

Primary pulmonary hypertension (PPH, now IPAH)

- pulmonary arterial pressure > 25 mmHg at rest, > 30mmHg with exercise
- PPH is diagnosed when no underlying cause can be found
- around 10% of cases are familial: autosomal dominant
- endothelin thought to play a key role in pathogenesis
- associated with HIV, cocaine and anorexigens (e.g. fenfluramine)

### Features

- more common in females, typically presents at 20-40 years old
- progressive SOB
- cyanosis
- right ventricular heave, loud P2, raised JVP with prominent 'a' waves, tricuspid regurgitation

### Investigation

- echocardiography

### Management

- diuretics if right heart failure
- anticoagulation
- vasodilator therapy: calcium channel blocker, IV prostaglandins, bosentan: endothelin-1 receptor antagonist
- heart-lung transplant

**Question 198 of 247**

Next

You review a 47-year-old man in clinic. He has been referred with difficult to control hypertension despite taking a combination of lisinopril, indapamide and amlodipine. Whilst examining the patient you note over 15 large café-au-lait spots on his trunk. Some axillary freckling is also present. His blood pressure (despite medication) is 170/94 mmHg and pulse 90/min.

Routine bloods are ordered:

Hb	15.2 g/dl
Platelets	$201 \times 10^9/l$
WBC	$5.2 \times 10^9/l$

Na <sup>+</sup>	141 mmol/l
K <sup>+</sup>	4.3 mmol/l
Urea	6.1 mmol/l
Creatinine	88 µmol/l

Urine dipstick is normal. Which one of the following investigations is most likely to be diagnostic?

<input type="radio"/>	A. MRI brain
<input type="radio"/>	B. 24 hr urinary cortisol
<input type="radio"/>	C. Glucose tolerance test with growth hormone measurements
<input type="radio"/>	D. Renal arteriography
<input type="radio"/>	E. 24 hr urinary collection of catecholamines

Patients with neurofibromatosis may develop hypertension for three main reasons:

- coexistent essential hypertension
- pheochromocytoma
- renal vascular stenosis secondary to fibromuscular dysplasia

The normal renal function in this patient points away from a diagnosis of renal vascular disease. Pheochromocytoma therefore needs to be excluded first.

**Neurofibromatosis**

There are two types of neurofibromatosis, NF1 and NF2. Both are inherited in an autosomal dominant fashion. NF1 is also known as von Recklinghausen's syndrome. It is caused by a gene mutation on chromosome 17 which encodes neurofibromin and affects around 1 in 4,000. NF2 is caused by gene mutation on chromosome 22 and affects around 1 in 100,000.

## Features

NF1	NF2
Café-au-lait spots ( $\geq 6$ , 15 mm in diameter) Axillary/groin freckles Peripheral neurofibromas Iris: Lisch nodules in $> 90\%$ Scoliosis	Bilateral acoustic neuromas

Next

### Question 199 of 247

A 65-year-old man is admitted with palpitations. The ECG shows a ventricular rate of 150/min with an underlying atrial rate of 300/min. A diagnosis of atrial flutter is suspected. What is the treatment of choice to permanently restore sinus rhythm?

<input type="radio"/>	A. Radiofrequency ablation of the accessory pathway
<input type="radio"/>	B. Radiofrequency ablation of the AV node
<input type="radio"/>	C. Radiofrequency ablation of the tricuspid valve isthmus
<input type="radio"/>	D. Lifelong amiodarone
<input type="radio"/>	E. Permanent pacemaker

[Next question](#)

### Atrial flutter

Atrial flutter is a form of supraventricular tachycardia characterised by a succession of rapid atrial depolarisation waves.

#### ECG findings

- 'sawtooth' appearance
- as the underlying atrial rate is often around 300/min the ventricular or heart rate is dependent on the degree of AV block. For example if there is 2:1 block the ventricular rate will be 150/min
- flutter waves may be visible following carotid sinus massage or adenosine

#### Management

- is similar to that of atrial fibrillation although medication may be less effective
- atrial flutter is more sensitive to cardioversion however so lower energy levels may be used
- radiofrequency ablation of the tricuspid valve isthmus is curative for most patients

[Next](#)

### Question 200 of 247

A 29-year-old man with myotonic dystrophy has an electrocardiogram. Which one of the following findings is most likely to be present?

<input type="radio"/>	A. Wide QRS complex
<input type="radio"/>	B. Atrial fibrillation
<input type="radio"/>	C. Voltage criteria for left ventricular hypertrophy
<input type="radio"/>	D. Right axis deviation
<input type="radio"/>	E. Prolonged PR interval

A prolonged PR interval is seen in around 20-40% of patients

### Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

#### Genetics

- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	DM2
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent - Severe congenital form not seen

#### General features

- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

#### Other features

- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus



- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia

A 35-year-old man who is an intravenous drug user is admitted to hospital. He has had three previous admissions with infective endocarditis but presents on this occasion feeling generally unwell, complaining of upper abdominal discomfort and leg swelling. On examination he has an elevated jugular venous pressure, tender hepatomegaly and peripheral oedema. A diagnosis of tricuspid regurgitation is suspected. Which one of the following additional features would be most supportive of this diagnosis?

<input type="radio"/>	A. Split first heart sound
<input type="radio"/>	B. Early diastolic murmur
<input type="radio"/>	C. Left parasternal heave
<input type="radio"/>	D. Wide pulse pressure
<input type="radio"/>	E. Cannon 'a' waves

[Next question](#)

### Tricuspid regurgitation

#### Signs

- pan-systolic murmur
- giant V waves in JVP
- pulsatile hepatomegaly
- left parasternal heave

#### Causes

- right ventricular dilation
- pulmonary hypertension e.g. COPD
- rheumatic heart disease
- infective endocarditis (especially intravenous drug users)
- Ebstein's anomaly
- carcinoid syndrome

A 55-year old man with a history of ischaemic heart disease presents to the Emergency Department with palpitations for the past 10 days. Examination of his pulse reveals a rate of 130 bpm which is irregularly irregular. He has had one previous episode of atrial fibrillation 3 months ago which was terminated by elective cardioversion following warfarinisation. What term best describes his arrhythmia?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Paroxysmal atrial fibrillation |
| <input type="radio"/> | B. Atrial flutter                 |
| <input type="radio"/> | C. Permanent atrial fibrillation  |
| <input type="radio"/> | D. Persistent atrial fibrillation |
| <input type="radio"/> | E. Secondary atrial fibrillation  |

[Next question](#)

### Atrial fibrillation: classification

An attempt was made in the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines to simplify and clarify the classification of atrial fibrillation (AF).

It is recommended that AF be classified into 3 patterns:

- first detected episode (irrespective of whether it is symptomatic or self-terminating)
- recurrent episodes, when a patient has 2 or more episodes of AF. If episodes of AF terminate spontaneously then the term **paroxysmal AF** is used. Such episodes last less than 7 days (typically < 24 hours). If the arrhythmia is not self-terminating then the term **persistent AF** is used. Such episodes usually last greater than 7 days
- in **permanent AF** there is continuous atrial fibrillation which cannot be cardioverted or if attempts to do so are deemed inappropriate. Treatment goals are therefore rate control and anticoagulation if appropriate

Which of the following is least associated with a poor prognosis in hypertrophic cardiomyopathy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Non-sustained ventricular tachycardia on 24 or 48-hour Holter monitoring |
| <input type="radio"/> | B. Reduced left ventricular outflow gradient                                |
| <input type="radio"/> | C. Family history of sudden death   |
| <input type="radio"/> | D. Syncope  |
| <input type="radio"/> | E. Early age at presentation  |

Next question

There is no recognised prognostic association with left ventricular outflow gradient

### **HOCM: prognostic factors**

Hypertrophic obstructive cardiomyopathy (HOCM) is an autosomal dominant disorder of muscle tissue caused by defects in the genes encoding contractile proteins. Mutations to various proteins including beta-myosin, alpha-tropomyosin and troponin T have been identified. Septal hypertrophy causes left ventricular outflow obstruction. It is an important cause of sudden death in apparently healthy individuals.

Poor prognostic factors

- syncope
- family history of sudden death
- young age at presentation
- non-sustained ventricular tachycardia on 24 or 48-hour Holter monitoring
- abnormal blood pressure changes on exercise

An increased septal wall thickness is also associated with a poor prognosis.

Which one of the following statements regarding arrhythmogenic right ventricular cardiomyopathy is correct?

<input type="radio"/>	A. Inherited in an autosomal recessive pattern
<input type="radio"/>	B. It is now the most common cause of sudden cardiac death in the UK
<input type="radio"/>	C. All patients should have an implantable cardioverter defibrillator fitted
<input type="radio"/>	D. It is characterised by fibrofatty infiltration of the right ventricular myocardium
<input type="radio"/>	E. Naxos disease is the association of arrhythmogenic right ventricular cardiomyopathy with deafness

Drug therapy is used in patients with well tolerated or non life-threatening ventricular arrhythmias.

### Arrhythmogenic right ventricular cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a form of inherited cardiovascular disease which may present with syncope or sudden cardiac death. It is generally regarded as the second most common cause of sudden cardiac death in the young after hypertrophic cardiomyopathy.

Pathophysiology

- inherited in an autosomal dominant pattern with variable expression
- the right ventricular myocardium is replaced by fibrofatty tissue

Presentation

- palpitations
- syncope
- sudden cardiac death

Investigation

- ECG abnormalities in V1-3, typically T wave inversion. An epsilon wave is found in about 50% of those with ARV - this is best described as a terminal notch in the QRS complex
- echo changes are often subtle in the early stages but may show an enlarged, hypokinetic right ventricle with a thin free wall
- magnetic resonance imaging is useful to show fibrofatty tissue

Management

- drugs: sotalol is the most widely used antiarrhythmic
- catheter ablation to prevent ventricular tachycardia
- implantable cardioverter-defibrillator

Naxos disease

- an autosomal recessive variant of ARVC
- a triad of ARVC, palmoplantar keratosis, and woolly hair

A 62-year-old female with a known history of a sigmoid adenocarcinoma is admitted to hospital with shortness of breath and pyrexia. On examination a murmur is heard and an echo reveals a vegetation on the aortic valve. Which one of the following organisms is most characteristically associated with causing infective endocarditis in patients with colorectal cancer?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. <i>Escherichia coli</i>      |
| <input type="radio"/> | B. <i>Enterococcus faecalis</i> |
| <input type="radio"/> | C. <i>Salmonella</i>            |
| <input type="radio"/> | D. <i>Campylobacter</i>         |
| <input type="radio"/> | E. <i>Streptococcus bovis</i>   |

[Next question](#)

*Streptococcus bovis* endocarditis is associated with colorectal cancer

### Infective endocarditis

The strongest risk factor for developing infective endocarditis is a previous episode of endocarditis. The following types of patients are affected:

- previously normal valves (50%, typically acute presentation)
- rheumatic valve disease (30%)
- prosthetic valves
- congenital heart defects
- intravenous drug users (IVDUs, e.g. Typically causing tricuspid lesion)

### Causes

- *Streptococcus viridans* (most common cause - 40-50%)
- *Staphylococcus epidermidis* (especially prosthetic valves)
- *Staphylococcus aureus* (especially acute presentation, IVDUs)
- *Streptococcus bovis* is associated with colorectal cancer
- non-infective: systemic lupus erythematosus (Libman-Sacks), malignancy: marantic endocarditis

### Culture negative causes

- prior antibiotic therapy
- *Coxiella burnetii*
- *Bartonella*
- *Brucella*
- HACEK: *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, *Kingella*)

Following prosthetic valve surgery *Staphylococcus epidermidis* is the most common organism in the first 2 months and is usually the result of perioperative contamination. After 2 months the spectrum of organisms which cause endocarditis return to normal, except with a slight increase in *Staph. aureus* infections

Next

### Question 206 of 247

The most common cause of restrictive cardiomyopathy in the UK is:

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Diabetes mellitus            |
| <input type="radio"/> | B. Systemic lupus erythematosus |
| <input type="radio"/> | C. Haemochromatosis             |
| <input type="radio"/> | D. Tuberculosis                 |
| <input type="radio"/> | E. Amyloidosis                  |

[Next question](#)

Restrictive cardiomyopathy: amyloid (most common), haemochromatosis, Loffler's syndrome, sarcoidosis, scleroderma

### Restrictive cardiomyopathy

#### Features

- similar to constrictive pericarditis

Features suggesting restrictive cardiomyopathy rather than constrictive pericarditis

- prominent apical pulse
- absence of pericardial calcification on CXR
- heart may be enlarged
- ECG abnormalities e.g. bundle branch block, Q waves

#### Causes

- amyloidosis (e.g. secondary to myeloma) - most common cause in UK
- haemochromatosis
- Loffler's syndrome
- sarcoidosis
- scleroderma

[Next](#)



### Question 207 of 247

Which of the following is a cause of a loud second heart sound?

<input type="radio"/>	A. Aortic regurgitation
<input type="radio"/>	B. Ventricular septal defect
<input type="radio"/>	C. Systemic hypertension
<input type="radio"/>	D. Aortic stenosis
<input type="radio"/>	E. Mitral stenosis

#### Second heart sound (S2)

- loud: hypertension
- soft: AS
- fixed split: ASD
- reversed split: LBBB

#### Heart sounds: S2

S2 is caused by the closure of the aortic valve (A2) closely followed by that of the pulmonary valve (P2)

Causes of a loud S2

- hypertension: systemic (loud A2) or pulmonary (loud P2)
- hyperdynamic states
- atrial septal defect without pulmonary hypertension

Causes of a soft S2

- aortic stenosis

Causes of fixed split S2

- atrial septal defect

Causes of a widely split S2

- deep inspiration
- RBBB
- pulmonary stenosis
- severe mitral regurgitation

Causes of a reversed (paradoxical) split S2 (P2 occurs before A2)

- LBBB

- severe aortic stenosis
- right ventricular pacing
- WPW type B (causes early P2)
- patent ductus arteriosus

Next

### Question 208 of 247

A 53-year-old man is reviewed in the cardiology clinic with a history of chest pain and syncope. On examination he has an ejection systolic murmur radiating to the carotid area. What is the most likely cause of his symptoms?

<input type="radio"/>	A. Bicuspid aortic valve
<input type="radio"/>	B. Aortic root abscess
<input type="radio"/>	C. Post rheumatic fever
<input type="radio"/>	D. Posterior myocardial infarction
<input type="radio"/>	E. Calcification of the aortic valve

[Next question](#)

Aortic stenosis - most common cause:

- younger patients < 65 years: bicuspid aortic valve
- older patients > 65 years: calcification

### Aortic stenosis

Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis

- degenerative calcification (most common cause in older patients > 65 years)
- bicuspid aortic valve (most common cause in younger patients < 65 years)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management

- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement

- if asymptomatic but valvular gradient  $> 50$  mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

Next

### Question 209 of 247

An 82-year-old man is reviewed. He is known to have ischaemic heart disease and is still getting regular attacks of angina despite taking atenolol 100mg od. Examination of his cardiovascular system is unremarkable with a pulse of 72 bpm and a blood pressure of 148/92 mmHg. What is the most appropriate next step in management?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. Add verapamil 80mg tds             |
| <input type="radio"/> | B. Add nicorandil 10mg bd             |
| <input type="radio"/> | C. Add diltiazem 60mg tds             |
| <input type="radio"/> | D. Add nifedipine MR 30mg od          |
| <input type="radio"/> | E. Add isosorbide mononitrate 30mg bd |

[Next question](#)

NICE guidelines recommend adding a calcium channel blocker for angina which is not adequately controlled with beta-blocker monotherapy. Verapamil is contraindicated whilst taking a beta-blocker and diltiazem should be used with caution due to the risk of bradycardia.

The starting dose of isosorbide mononitrate is 10mg bd.

### Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery. NICE produced guidelines in 2011 covering the management of stable angina

#### Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- NICE recommend using either a beta-blocker or a calcium channel blocker first-line based on 'comorbidities, contraindications and the person's preference'
- if a calcium channel blocker is used as monotherapy a rate-limiting one such as verapamil or diltiazem should be used. If used in combination with a beta-blocker then use a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine). Remember that beta-blockers should not be prescribed concurrently with verapamil (risk of complete heart block)
- if there is a poor response to initial treatment then medication should be increased to the maximum tolerated dose (e.g. for atenolol 100mg od)
- if a patient is still symptomatic after monotherapy with a beta-blocker add a calcium channel blocker and vice versa
- if a patient is on monotherapy and cannot tolerate the addition of a calcium channel blocker or a beta-blocker then consider one of the following drugs: a long-acting nitrate, ivabradine, nicorandil or ranolazine
- if a patient is taking both a beta-blocker and a calcium-channel blocker then only add a third drug whilst a patient is awaiting assessment for PCI or CABG

## Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy
- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

## Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the  $I_f$  ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

Next

### Question 210 of 247

A 58-year-old man presents to the Emergency Department following an episode of transient right-sided weakness which lasted approximately 20 minutes. He has had two previous episodes of a similar nature. On examination he is found to be in atrial fibrillation at a rate of 80 bpm.

CT head    normal

He is started on aspirin 300mg od. Two days later he has a carotid doppler which is normal. What is the most appropriate management?

- ☐ A. Start digoxin
- ☐ B. Switch to aspirin 300mg od + dipyridamole 200mg bd long-term
- ☐ C. Wait two weeks from the date of the last event then switch from aspirin to warfarin
- ☐ D. Switch to aspirin 75mg od long-term
- ☐ E. Start warfarin

[Next question](#)

This patient has atrial fibrillation. As a consequence he has had a number of transient ischaemic attacks (TIAs) and hence needs to be anticoagulated with warfarin.

In patients who've had an ischaemic stroke the guidelines recommend waiting two weeks before anticoagulation is commenced to reduce the risk of haemorrhagic transformation. However, NICE recommend for TIA patients: 'in the absence of cerebral infarction or haemorrhage, anticoagulation therapy should begin as soon as possible.'

### Atrial fibrillation: anticoagulation

The European Society of Cardiology published updated guidelines on the management of atrial fibrillation in 2012. They suggest using the **CHA<sub>2</sub>DS<sub>2</sub>-VASc** score to determine the most appropriate anticoagulation strategy. This scoring system superceded the CHADS<sub>2</sub>score.

	Condition	Points
<b>C</b>	Congestive heart failure	1
<b>H</b>	Hypertension (or treated hypertension)	1
<b>A<sub>2</sub></b>	Age >= 75 years	2
<b>D</b>	Diabetes	1
<b>S<sub>2</sub></b>	Prior Stroke or TIA	2
<b>V</b>	Vascular disease (including ischaemic heart disease and peripheral arterial disease)	1
<b>A</b>	Age 65-74 years	1
<b>S</b>	Sex (female)	1

The table below shows a suggested anticoagulation strategy\* based on the score:

Score	Anticoagulation
0	No treatment is preferred to aspirin
1	Oral anticoagulants preferred to aspirin; dabigatran is an alternative
2 or more	Oral anticoagulants; dabigatran is an alternative

\*the wording in the guidelines ('is preferred to') can be slightly confusing. It basically means that, say for a score of 0, whilst aspirin is an acceptable management option the weight of the clinical evidence would support no treatment instead

Next



### Question 211 of 247

Which one of the following clinical signs would best indicate severe calcified aortic stenosis?

<input type="radio"/>	A. Loudness of murmur
<input type="radio"/>	B. Loud second heart sound
<input type="radio"/>	C. Radiation to the carotids
<input type="radio"/>	D. Hypertension
<input type="radio"/>	E. Displaced apex beat

[Next question](#)

The apex beat is not normally displaced in aortic stenosis. Displacement would indicate left ventricular dilatation and hence severe disease

### Aortic stenosis

Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis

- degenerative calcification (most common cause in older patients > 65 years)
- bicuspid aortic valve (most common cause in younger patients < 65 years)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management

- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

A 51-year-old man presents four weeks after being discharged from hospital. He had been admitted with chest pain and thrombolysed for a myocardial infarction. This morning he developed marked tongue and facial swelling. Which one of the following drugs is most likely to be responsible?

<input type="radio"/>	A. Atorvastatin
<input type="radio"/>	B. Isosorbide mononitrate
<input type="radio"/>	C. Atenolol
<input type="radio"/>	D. Aspirin
<input type="radio"/>	E. Ramipril

ACE inhibitors are the most common cause of drug-induced angioedema.

### Angiotensin-converting enzyme inhibitors

Angiotensin-converting enzyme (ACE) inhibitors are now the established first-line treatment in younger patients with hypertension and are also extensively used to treat heart failure. They are known to be less effective in treating hypertensive Afro-Caribbean patients. ACE inhibitors are also used to treat diabetic nephropathy and have a role in secondary prevention of ischaemic heart disease.

Mechanism of action:

- inhibit the conversion angiotensin I to angiotensin II

Side-effects:

- cough: occurs in around 15% of patients and may occur up to a year after starting treatment. Thought to be due to increased bradykinin levels
- angioedema: may occur up to a year after starting treatment
- hyperkalaemia
- first-dose hypotension: more common in patients taking diuretics

Cautions and contraindications

- pregnancy and breastfeeding - avoid
- renovascular disease - significant renal impairment may occur in patients who have undiagnosed bilateral renal artery stenosis
- aortic stenosis - may result in hypotension
- patients receiving high-dose diuretic therapy (more than 80 mg of furosemide a day) - significantly increases the risk of hypotension
- hereditary or idiopathic angioedema

Monitoring

- urea and electrolytes should be checked before treatment is initiated and after increasing the dose

- a rise in the creatinine and potassium may be expected after starting ACE inhibitors. Acceptable changes are an increase in serum creatinine, up to 30%\* from baseline and an increase in potassium up to 5.5 mmol/l\*.

\*Renal Association UK, Clinical Knowledge Summaries quote 50% which seems rather high. SIGN advise that the fall in eGFR should be less than 20%. The NICE CKD guidelines suggest that a decrease in eGFR of up to 25% or a rise in creatinine of up to 30% is acceptable

Next

### Question 213 of 247

A 24-year-old female develops transient slurred speech following a flight from Australia to the United Kingdom. Both a CT head and ECG are normal. Which one of the following tests is most likely to reveal the underlying cause?

<input type="radio"/>	A. Transoesophageal echo
<input type="radio"/>	B. MRI brain
<input type="radio"/>	C. Carotid USS Doppler
<input type="radio"/>	D. Cerebral angiogram
<input type="radio"/>	E. Transthoracic echo

[Next question](#)

Paradoxical embolus - PFO most common cause - do TOE

Transesophageal echocardiography provides superior views of the atrial septum and therefore is preferred to transthoracic echocardiography for detecting patent foramen ovale

#### Paradoxical embolisation

For a right-sided thrombus (e.g. DVT) to cause a left-sided embolism (e.g. stroke) it must obviously pass from the right-to-left side of the heart

The following cardiac lesions may cause such events

- patent foramen ovale - present in around 20% of the population
- atrial septal defect - a much less common cause

[Next](#)

### Question 214 of 247

A 42-year-old man of Afro-Caribbean origin is diagnosed as having hypertension. Secondary causes of hypertension have been excluded. What is the most appropriate initial drug therapy?

- ☐ A. Losartan
- ☐ B. Bisoprolol
- ☐ C. Indapamide
- ☐ D. Ramipril
- ☐ E. Amlodipine

[Next question](#)

ACE inhibitors have reduced efficacy in black patients and are therefore not used first-line

### Hypertension: diagnosis and management

NICE published updated guidelines for the management of hypertension in 2011. Some of the key changes include:

- classifying hypertension into stages
- recommending the use of ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM)
- calcium channel blockers are now considered superior to thiazides
- bendroflumethiazide is no longer the thiazide of choice

### Blood pressure classification

This becomes relevant later in some of the management decisions that NICE advocate.

<b>Stage 1 hypertension</b>	Clinic BP $\geq$ 140/90 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 135/85 mmHg
<b>Stage 2 hypertension</b>	Clinic BP $\geq$ 160/100 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 150/95 mmHg
<b>Severe hypertension</b>	Clinic systolic BP $\geq$ 180 mmHg, or clinic diastolic BP $\geq$ 110 mmHg

### Diagnosing hypertension

If a BP reading is  $\geq$  140 / 90 mmHg patients should be offered ABPM to confirm the diagnosis.

Patients with a BP reading of  $\geq$  180/110 mmHg should be considered for immediate treatment.

### Ambulatory blood pressure monitoring (ABPM)

- at least 2 measurements per hour during the person's usual waking hours (for example, between 08:00 and 22:00)
- use the average value of at least 14 measurements

If ABPM is not tolerated or declined HBPM should be offered.

### Home blood pressure monitoring (HBPM)

- for each BP recording, two consecutive measurements need to be taken, at least 1 minute apart and with the person seated
- BP should be recorded twice daily, ideally in the morning and evening
- BP should be recorded for at least 4 days, ideally for 7 days
- discard the measurements taken on the first day and use the average value of all the remaining measurements

## Managing hypertension

ABPM/HBPM  $\geq$  135/85 mmHg (i.e. stage 1 hypertension)

- treat if  $< 80$  years of age and any of the following apply; target organ damage, established cardiovascular disease, renal disease, diabetes or a 10-year cardiovascular risk equivalent to 20% or greater

ABPM/HBPM  $\geq$  150/95 mmHg (i.e. stage 2 hypertension)

- offer drug treatment regardless of age

For patients  $< 40$  years consider specialist referral to exclude secondary causes.

### Step 1 treatment

- patients  $< 55$ -years-old: ACE inhibitor (A)
- patients  $> 55$ -years-old or of Afro-Caribbean origin: calcium channel blocker

### Step 2 treatment

- ACE inhibitor + calcium channel blocker (A + C)

### Step 3 treatment

- add a thiazide diuretic (D, i.e. A + C + D)

- NICE now advocate using either chlorthalidone (12.5-25.0 mg once daily) or indapamide (1.5 mg modified-release once daily or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide

NICE define a clinic BP  $\geq 140/90$  mmHg after step 3 treatment with optimal or best tolerated doses as resistant hypertension. They suggest step 4 treatment or seeking expert advice

#### Step 4 treatment

- consider further diuretic treatment
- if potassium  $< 4.5$  mmol/l add spironolactone 25mg od
- if potassium  $> 4.5$  mmol/l add higher-dose thiazide-like diuretic treatment
- if further diuretic therapy is not tolerated, or is contraindicated or ineffective, consider an alpha- or beta-blocker

If BP still not controlled seek specialist advice.

#### Blood pressure targets

	Clinic BP	ABPM / HBPM
Age $< 80$ years	140/90 mmHg	135/85 mmHg
Age $> 80$ years	150/90 mmHg	145/85 mmHg

#### New drugs

##### Direct renin inhibitors

- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

A 17-year-old girl with Turner's syndrome is reviewed in the cardiology clinic. Other than coarctation of the aorta, what is the most common cardiac abnormality found in patients with Turner's syndrome?

<input type="radio"/>	A. Ventricular septal defect
<input checked="" type="radio"/>	B. Bicuspid aortic valve
<input type="radio"/>	C. Aortic stenosis
<input type="radio"/>	D. Pulmonary stenosis
<input type="radio"/>	E. Partial anomalous venous drainage

[Next question](#)

Up to 15% of adults with Turner's syndrome have bicuspid aortic valves

### Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

#### Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease



A 67-year-old man is admitted with palpitations. During examination of his JVP he is noted to have regular cannon waves. Which one of the following arrhythmias is most likely to be responsible for this finding?

<input type="radio"/>	A. Atrio-ventricular nodal re-entry tachycardia
<input type="radio"/>	B. Atrial fibrillation
<input type="radio"/>	C. Atrial flutter
<input type="radio"/>	D. Complete heart block
<input type="radio"/>	E. Ventricular fibrillation

[Next question](#)

Atrio-ventricular nodal re-entry tachycardia and ventricular tachycardia with 1:1 ventricular-atrial conduction may produce regular cannon waves. Complete heart block causes irregular cannon waves

#### JVP: cannon waves

Caused by the right atrium contracting against a closed tricuspid valve. May be subdivided into regular or intermittent

Regular cannon waves

- ventricular tachycardia (with 1:1 ventricular-atrial conduction)
- atrio-ventricular nodal re-entry tachycardia (AVNRT)

Irregular cannon waves

- complete heart block

### Question 217 of 247

A 75-year-old woman is brought to the Emergency Department by her family. She has been getting more short-of-breath over the last 6 weeks and says her energy levels are low. An ECG on arrival shows atrial fibrillation at a rate of 114 / min. Blood pressure is 128/80 mmHg and a chest x-ray is unremarkable. What is the appropriate drug to control the heart rate?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Felodipine |
| <input type="radio"/> | B. Amiodarone |
| <input type="radio"/> | C. Digoxin    |
| <input type="radio"/> | D. Flecainide |
| <input type="radio"/> | E. Bisoprolol |

Atrial fibrillation: rate control - beta blockers preferable to digoxin

This question reiterates an important point which frequently comes up in exams - digoxin is no longer first-line for rate control in atrial fibrillation. Her shortness-of-breath is likely to be rate related and does not necessarily mean that she is in heart failure. This is supported by a normal chest x-ray.

Please see the NICE guidelines for further information.

#### Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
Older than 65 years History of ischaemic heart disease	Younger than 65 years Symptomatic First presentation Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) Congestive heart failure

Next

### Question 218 of 247

A 75-year-old woman is reviewed following a 'collapse' yesterday. Her husband found her unconscious on the bathroom floor and describes her 'quickly coming round'. What is the most likely cause of collapse in this patient?

<input type="radio"/>	A. Orthostatic syncope
<input type="radio"/>	B. Cardiac syncope
<input type="radio"/>	C. Reflex syncope
<input type="radio"/>	D. Drug-induced syncope
<input type="radio"/>	E. Unexplained

[Next question](#)

Reflex syncope is the most common cause of syncope in all age groups although orthostatic and cardiac causes become progressively more common in older patients

### Syncope

Syncope may be defined as a transient loss of consciousness due to global cerebral hypoperfusion with rapid onset, short duration and spontaneous complete recovery. Note how this definition excludes other causes of collapse such as epilepsy.

The European Society of Cardiology published guidelines in 2009 on the investigation and management of syncope. They suggested the following classification:

Reflex syncope (neurally mediated)

- vasovagal: triggered by emotion, pain or stress. Often referred to as 'fainting'
- situational: cough, micturition, gastrointestinal
- carotid sinus syncope

Orthostatic syncope

- primary autonomic failure: Parkinson's disease, Lewy body dementia
- secondary autonomic failure: e.g. Diabetic neuropathy, amyloidosis, uraemia
- drug-induced: diuretics, alcohol, vasodilators
- volume depletion: haemorrhage, diarrhoea

Cardiac syncope

- arrhythmias: bradycardias (sinus node dysfunction, AV conduction disorders) or tachycardias (supraventricular, ventricular)
- structural: valvular, myocardial infarction, hypertrophic obstructive cardiomyopathy
- others: pulmonary embolism

Reflex syncope is the most common cause in all age groups although orthostatic and cardiac causes become progressively more common in older patients.

#### Evaluation

- cardiovascular examination
- postural blood pressure readings: a symptomatic fall in systolic BP  $> 20$  mmHg or diastolic BP  $> 10$  mmHg or decrease in systolic BP  $< 90$  mmHg is considered diagnostic
- ECG
- carotid sinus massage
- tilt table test
- 24 hour ECG

Next

### Question 219 of 247

A 76-year-old woman is admitted to the resus department after collapsing whilst shopping. The paramedics report she is hypotensive and tachycardia. Initial observations include a heart rate of 160 bpm and a blood pressure of 98 / 60 mmHg. A 12 lead ECG shows a broad complex tachycardia. Which one of the following features on the ECG would suggest a ventricular tachycardia rather than a supraventricular tachycardia with aberrant conduction?

<input type="radio"/>	A. QRS < 160 ms
<input type="radio"/>	B. A corrected QT interval of 420ms
<input type="radio"/>	C. Atrioventricular dissociation
<input type="radio"/>	D. Marked right axis deviation
<input type="radio"/>	E. Heart rate of 160 bpm

#### Broad complex tachycardia

Features suggesting VT rather than SVT with aberrant conduction

- AV dissociation
- fusion or capture beats
- positive QRS concordance in chest leads
- marked left axis deviation
- history of IHD
- lack of response to adenosine or carotid sinus massage
- QRS > 160 ms

Next

### Question 220 of 247

A 30-year-old woman is admitted to the Emergency Department following the acute onset of palpitations. Blood pressure is 124/84 mmHg and her pulse is 150/min. An ECG shows a narrow complex tachycardia. Intravenous access is gained and 6mg of adenosine is given with no effect. What is the most appropriate next step?

<input type="radio"/>	A. Intravenous adenosine 12 mg
<input type="radio"/>	B. Intravenous adenosine 6mg
<input type="radio"/>	C. Intravenous verapamil 2.5-5 mg
<input type="radio"/>	D. Radio-frequency ablation
<input type="radio"/>	E. Electrical cardioversion

Next question

A further dose of adenosine should be given if there is no response to the initial injection. Please see the Resuscitation Council (UK) link for further details.

### Supraventricular tachycardia

Whilst strictly speaking the term supraventricular tachycardia (SVT) refers to any tachycardia that is not ventricular in origin the term is generally used in the context of paroxysmal SVT. Episodes are characterised by the sudden onset of a narrow complex tachycardia, typically an atrioventricular nodal re-entry tachycardia (AVNRT). Other causes include atrioventricular re-entry tachycardias (AVRT) and junctional tachycardias.

#### Acute management

- vagal manoeuvres: e.g. Valsalva manoeuvre
- intravenous adenosine: contraindicated in asthmatics - verapamil is a preferable option
- electrical cardioversion

#### Prevention of episodes

- beta-blockers
- radio-frequency ablation

A 60-year-old man is admitted following an acute coronary syndrome. He receives aspirin, clopidogrel, nitrates and morphine. His 6-month risk score is high and percutaneous coronary intervention is planned. He is therefore given intravenous tirofiban. What is the mechanism of action of this drug?

- ☐ A. Inhibits the production of thromboxane A<sub>2</sub>
- ☐ B. Activates antithrombin III
- ☐ C. Coronary vasodilator
- ☐ D. Glycoprotein IIb/IIIa receptor antagonist
- ☐ E. Reversible direct thrombin inhibitor

### Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive

- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

**Antithrombin** treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patient's creatinine is > 265 µmol/l unfractionated heparin should be given.

**Clopidogrel** 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

**Coronary angiography** should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:



<b>Aspirin</b>	Antiplatelet - inhibits the production of thromboxane A2
<b>Clopidogrel</b>	Antiplatelet - inhibits ADP binding to its platelet receptor
<b>Enoxaparin</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Fondaparinux</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Bivalirudin</b>	Reversible direct thrombin inhibitor

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### Question 222 of 247

A 65-year-old female is admitted with a suspected infective exacerbation of chronic obstructive pulmonary disease. On examination she is dyspnoeic with a blood pressure of 112/68 mmHg. Electrocardiogram shows an irregular, narrow-complex tachycardia with a rate of 130 bpm. At least three different P wave morphologies are seen. A diagnosis of multifocal tachycardia is suspected. What is the most appropriate management?

<input type="radio"/>	A. Adenosine
<input type="radio"/>	B. Digoxin
<input type="radio"/>	C. Verapamil
<input type="radio"/>	D. Atenolol
<input type="radio"/>	E. DC cardioversion

[Next question](#)

### Multifocal atrial tachycardia

Multifocal atrial tachycardia (MAT) may be defined as a irregular cardiac rhythm caused by at least three different sites in the atria, which may be demonstrated by morphologically distinctive P waves. It is more common in elderly patients with chronic lung disease, for example COPD

#### Management

- correction of hypoxia and electrolyte disturbances
- rate-limiting calcium channel blockers are often used first-line
- cardioversion and digoxin are not useful in the management of MAT

[Next](#)

### Question 223 of 247

Which one of the following treatments is not appropriate in the management of Wolff-Parkinson White?

<input type="radio"/>	A. Verapamil
<input type="radio"/>	B. Sotalol
<input type="radio"/>	C. Amiodarone
<input type="radio"/>	D. Flecainide
<input type="radio"/>	E. Radiofrequency ablation of the accessory pathway

Verapamil and digoxin should be avoided in patients with Wolff-Parkinson White as they may precipitate VT or VF

### Wolff-Parkinson White

Wolff-Parkinson White (WPW) syndrome is caused by a congenital accessory conducting pathway between the atria and ventricles leading to a atrioventricular re-entry tachycardia (AVRT). As the accessory pathway does not slow conduction AF can degenerate rapidly to VF

Possible ECG features include:

- short PR interval
- wide QRS complexes with a slurred upstroke - 'delta wave'
- left axis deviation if right-sided accessory pathway\*
- right axis deviation if left-sided accessory pathway\*

Differentiating between type A and type B

- type A (left-sided pathway): dominant R wave in V1
- type B (right-sided pathway): no dominant R wave in V1

Associations of WPW

- HOCM
- mitral valve prolapse
- Ebstein's anomaly
- thyrotoxicosis
- secundum ASD

Management

- definitive treatment: radiofrequency ablation of the accessory pathway
- medical therapy: sotalol\*\*, amiodarone, flecainide

\*in the majority of cases, or in a question without qualification, Wolff-Parkinson-White syndrome is associated with left axis deviation

\*\*sotalol should be avoided if there is coexistent atrial fibrillation as prolonging the refractory period at the AV

node may increase the rate of transmission through the accessory pathway, increasing the ventricular rate and potentially deteriorating into ventricular fibrillation

Next

### Question 224 of 247

A 65-year-old man is discharged from hospital following a thrombolysed ST-elevation myocardial infarction. Other than a history of depression he has no past medical history of note. His stay on the coronary care unit was complicated by the development of dyspnoea and an echo show a reduced left ventricular ejection fraction. The patient was not given clopidogrel during his hospital admission. Other than standard treatment with an ACE inhibitor, beta-blocker, aspirin and statin, what other type of drug should he be taking?

<input type="radio"/>	A. Angiotensin 2 receptor antagonist
<input type="radio"/>	B. Potassium channel activator
<input type="radio"/>	C. Aldosterone antagonist
<input type="radio"/>	D. Thiazide diuretic
<input type="radio"/>	E. Clopidogrel

An aldosterone antagonist is recommended by current NICE guidelines as the patient has a reduced left ventricular ejection fraction. If clopidogrel was given during the first 24 hours then it should be continued for the next 4 weeks

#### Myocardial infarction: secondary prevention

NICE produced guidelines on the management of patients following a myocardial infarction (MI) in 2007. Some key points are listed below

All patients should be offered the following drugs:

- ACE inhibitor
- beta-blocker
- aspirin
- statin

#### Clopidogrel

- ST-segment-elevation MI: patients treated with a combination of aspirin and clopidogrel during the first 24 hours after the MI should continue this treatment for at least 4 weeks
- non-ST segment elevation myocardial infarction (NSTEMI): following the 2010 NICE unstable angina and NSTEMI guidelines clopidogrel should be given for the first 12 months if the 6 month mortality risk\* is > 1.5%

#### Aldosterone antagonists

- patients who have had an acute MI and who have symptoms and/or signs of heart failure and left ventricular systolic dysfunction, treatment with an aldosterone antagonist licensed for post-MI treatment (e.g. eplerenone) should be initiated within 3-14 days of the MI, preferably after ACE inhibitor therapy

\*this can be calculated using scoring systems such as GRACE

### Question 225 of 247

A 62-year-old man who had a mechanical mitral valve replacement four years ago is reviewed. What long term antithrombotic therapy is he likely to be taking?

- ☐ A. Nothing
- ☐ B. Warfarin
- ☐ C. Aspirin
- ☐ D. Aspirin + clopidogrel for the first 12 months
- ☐ E. Warfarin + aspirin

[Next question](#)

Prosthetic heart valves - antithrombotic therapy:

- bioprosthetic: aspirin
- mechanical: warfarin + aspirin

### Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	Mechanical valves
Usually bovine or porcine in origin	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays
Major disadvantage is structural deterioration and calcification over time. Most older patients (> 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve	Mechanical valves have a low failure rate
Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication.
	Target INR <ul style="list-style-type: none"><li>• aortic: 2.0-3.0</li><li>• mitral: 2.5-3.5</li></ul>

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.

Which one of the following conditions is most associated with angiodysplasia?

<input type="radio"/>	A. Aortic regurgitation
<input type="radio"/>	B. Ventricular septal defect
<input type="radio"/>	C. Aortic stenosis
<input type="radio"/>	D. Hypertrophic obstructive cardiomyopathy
<input type="radio"/>	E. Mitral regurgitation

Next question

Angiodysplasia is associated with aortic stenosis

The association between angiodysplasia and aortic stenosis is thought to be caused by von Willebrand factor (vWF) being proteolysed in the turbulent blood flow around the aortic valve.

vWF is most active in vascular beds with high shear stress, such as angiodysplasia, and deficiency of vWF increases the bleeding risk from such lesions.

### Angiodysplasia

Angiodysplasia is a vascular deformity of the gastrointestinal tract which predisposes to bleeding and iron deficiency anaemia. There is thought to be an association with aortic stenosis, although this is debated. Angiodysplasia is generally seen in elderly patients

#### Diagnosis

- colonoscopy
- mesenteric angiography if acutely bleeding

#### Management

- endoscopic cautery or argon plasma coagulation
- antifibrinolytics e.g. Tranexamic acid
- oestrogens may also be used

A 65-year-old man admitted to the Acute Medical Unit is noted to have cannon 'a' waves of his jugular venous pressure during cardiovascular examination. Which one of the following would not cause this finding?

<input type="radio"/>	A. Tricuspid stenosis
<input type="radio"/>	B. Complete heart block
<input type="radio"/>	C. Ventricular tachycardia
<input type="radio"/>	D. Single chamber ventricular pacing
<input type="radio"/>	E. Nodal rhythm

[Next question](#)

Whilst tricuspid stenosis may cause large 'a' waves it does not cause cannon 'a' waves

### Jugular venous pulse

As well as providing information on right atrial pressure, the jugular vein waveform may provide clues to underlying valvular disease. A non-pulsatile JVP is seen in superior vena caval obstruction. Kussmaul's sign describes a paradoxical rise in JVP during inspiration seen in constrictive pericarditis.

'a' wave = atrial contraction

- large if atrial pressure e.g. tricuspid stenosis, pulmonary stenosis, pulmonary hypertension
- absent if in atrial fibrillation

Cannon 'a' waves

- caused by atrial contractions against a closed tricuspid valve
- are seen in complete heart block, ventricular tachycardia/ectopics, nodal rhythm, single chamber ventricular pacing

'c' wave

- closure of tricuspid valve
- not normally visible

'v' wave

- due to passive filling of blood into the atrium against a closed tricuspid valve
- giant v waves in tricuspid regurgitation

'x' descent = fall in atrial pressure during ventricular systole

'y' descent = opening of tricuspid valve



Which of the following is responsible for the early repolarisation phase of the myocardial action potential?

- ☐ A. Rapid sodium influx
- ☐ B. Rapid calcium influx
- ☐ C. Slow sodium efflux
- ☐ D. Slow efflux of calcium
- ☐ E. Efflux of potassium

Next question

## Electrical activity of the heart

### Myocardial action potential

Phase	Description	Mechanism
0	Rapid depolarisation	Rapid sodium influx These channels automatically deactivate after a few ms
1	Early repolarisation	Efflux of potassium
2	Plateau	Slow influx of calcium
3	Final repolarisation	Efflux of potassium
4	Restoration of ionic concentrations	Resting potential is restored by $\text{Na}^+/\text{K}^+$ ATPase There is slow entry of $\text{Na}^+$ into the cell decreasing the potential difference until the threshold potential is reached, triggering a new action potential

NB cardiac muscle remains contracted 10-15 times longer than skeletal muscle

### Conduction velocity

Atrial conduction	Spreads along ordinary atrial myocardial fibres at 1 m/sec
AV node conduction	0.05 m/sec
Ventricular conduction	Purkinje fibres are of large diameter and achieve velocities of 2-4 m/sec (this allows a rapid and coordinated contraction of the ventricles)

A 45-year-old man presents with pleuritic central chest pain. Which one of the following ECG findings is most specific for pericarditis?

<input type="radio"/>	A. PR depression
<input type="radio"/>	B. T wave inversion
<input type="radio"/>	C. Short PR interval
<input type="radio"/>	D. U waves
<input type="radio"/>	E. ST elevation

[Next question](#)

ST elevation is seen but is not specific as it may also indicate ischaemia

## Pericarditis

Pericarditis is one of the differentials of any patient presenting with chest pain.

### Features

- chest pain: may be pleuritic. Is often relieved by sitting forwards
- other symptoms include non-productive cough, dyspnoea and flu-like symptoms
- pericardial rub
- tachypnoea
- tachycardia

### Causes

- viral infections (Coxsackie)
- tuberculosis
- uraemia (causes 'fibrinous' pericarditis)
- trauma
- post-myocardial infarction, Dressler's syndrome
- connective tissue disease
- hypothyroidism

### ECG changes

- widespread 'saddle-shaped' ST elevation
- PR depression

A 78-year-old man with a four month history of exertional chest pain is reviewed. The pain typically comes on when he is walking up a hill, is centrally located and radiates to the left arm. It then settles with rest after about 2-3 minutes. Clinical examination and a resting 12 lead ECG are normal. Following NICE guidelines, what is the most appropriate diagnostic strategy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. CT calcium scoring                                     |
| <input type="radio"/> | B. Manage as angina, no further diagnostic tests required |
| <input type="radio"/> | C. Exercise tolerance test                                |
| <input type="radio"/> | D. MPS with SPECT   |
| <input type="radio"/> | E. Coronary angiography                                   |

[Next question](#)

NICE do not recommend any further investigation for patients with an estimated coronary artery disease risk of greater than 90%. This includes all men over the age of 70 years who have typical symptoms.

### Chest pain: assessment of patients with suspected cardiac chest pain

NICE issued guidelines in 2010 on the 'Assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin'.

Below is a brief summary of the key points. Please see the link for more details.

### Patients presenting with acute chest pain

Immediate management of suspected acute coronary syndrome (ACS)

- glyceryl trinitrate
- aspirin 300mg. NICE do not recommend giving other antiplatelet agents (i.e. Clopidogrel) outside of hospital
- do not routinely give oxygen, only give if sats < 94%\*
- perform an ECG as soon as possible but do not delay transfer to hospital. A normal ECG does not exclude ACS

### Referral

- current chest pain or chest pain in the last 12 hours with an abnormal ECG: emergency admission
- chest pain 12-72 hours ago: refer to hospital the same-day for assessment
- chest pain > 72 hours ago: perform full assessment with ECG and troponin measurement before deciding upon further action

\*NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO<sub>2</sub>) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO<sub>2</sub> of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO<sub>2</sub> of 88-92% until blood gas analysis is available.

## Patients presenting with stable chest pain

With all due respect to NICE the guidelines for assessment of patients with stable chest pain are rather complicated. They suggest an approach where the risk of a patient having coronary artery disease (CAD) is calculated based on their symptoms (whether they have typical angina, atypical angina or non-anginal chest pain), age, gender and risk factors.

NICE define anginal pain as the following:

- 1. constricting discomfort in the front of the chest, neck, shoulders, jaw or arms
- 2. precipitated by physical exertion
- 3. relieved by rest or GTN in about 5 minutes
- patients with all 3 features have typical angina
- patients with 2 of the above features have atypical angina
- patients with 1 or none of the above features have non-anginal chest pain

The risk tables are not reproduced here but can be found by clicking on the link.

If patients have typical anginal symptoms and a risk of CAD is greater than 90% then no further diagnostic testing is required. It should be noted that all men over the age of 70 years who have typical anginal symptoms fall into this category.

For patients with an estimated risk of 10-90% the following investigations are recommended. Note the absence of the exercise tolerance test:

Estimated likelihood of CAD	Diagnostic testing
61-90%	Coronary angiography
30-60%	Functional imaging, for example: <ul style="list-style-type: none"> <li>• myocardial perfusion scan with SPECT</li> <li>• stress echocardiography</li> <li>• first-pass contrast-enhanced magnetic resonance (MR) perfusion</li> <li>• MR imaging for stress-induced wall motion abnormalities.</li> </ul>
10-29%	CT calcium scoring

Dilated cardiomyopathy may be caused by deficiency of which one of the following:

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Chromium   |
| <input type="radio"/> | B. Magnesium  |
| <input type="radio"/> | C. Pyridoxine |
| <input type="radio"/> | D. Molybdenum |
| <input type="radio"/> | E. Selenium   |

### Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) basics

- dilated heart leading to systolic (+/- diastolic) dysfunction
- all 4 chambers affected but LV more so than RV
- features include arrhythmias, emboli, mitral regurgitation
- absence of congenital, valvular or ischaemic heart disease

Causes often considered separate entities

- alcohol: may improve with thiamine
- postpartum
- hypertension

Other causes

- inherited (see below)
- infections e.g. Coxsackie A and B, HIV, diphtheria, parasitic
- endocrine e.g. Hyperthyroidism
- infiltrative\* e.g. Haemochromatosis, sarcoidosis
- neuromuscular e.g. Duchenne muscular dystrophy
- nutritional e.g. Kwashiorkor, pellagra, thiamine/selenium deficiency
- drugs e.g. Doxorubicin

Inherited dilated cardiomyopathy

- around a third of patients with DCM are thought to have a genetic predisposition
- a large number of heterogeneous defects have been identified
- the majority of defects are inherited in an autosomal dominant fashion although other patterns of inheritance are seen

\*these causes may also lead to restrictive cardiomyopathy

A 72-year-old man is started on amlodipine 5mg od for hypertension. He has no other past medical history of note and routine bloods (including fasting glucose) and ECG were normal. What should his target blood pressure (based on clinic readings) be once on treatment?

- ☐ A. 130/80 mmHg
- ☐ B. 140/80 mmHg
- ☐ C. 140/85 mmHg
- ☐ D. 140/90 mmHg
- ☐ E. 150/90 mmHg

Next question

Blood pressure target (based on clinic readings) for patients < 80 years - 140/90 mmHg

### Hypertension: diagnosis and management

NICE published updated guidelines for the management of hypertension in 2011. Some of the key changes include:

- classifying hypertension into stages
- recommending the use of ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM)
- calcium channel blockers are now considered superior to thiazides
- bendroflumethiazide is no longer the thiazide of choice

### Blood pressure classification

This becomes relevant later in some of the management decisions that NICE advocate.

<b>Stage 1 hypertension</b>	Clinic BP $\geq$ 140/90 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 135/85 mmHg
<b>Stage 2 hypertension</b>	Clinic BP $\geq$ 160/100 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 150/95 mmHg
<b>Severe hypertension</b>	Clinic systolic BP $\geq$ 180 mmHg, or clinic diastolic BP $\geq$ 110 mmHg

### Diagnosing hypertension

If a BP reading is  $\geq$  140 / 90 mmHg patients should be offered ABPM to confirm the diagnosis.

Patients with a BP reading of  $\geq$  180/110 mmHg should be considered for immediate treatment.

### Ambulatory blood pressure monitoring (ABPM)

- at least 2 measurements per hour during the person's usual waking hours (for example, between 08:00 and 22:00)
- use the average value of at least 14 measurements

If ABPM is not tolerated or declined HBPM should be offered.

### Home blood pressure monitoring (HBPM)

- for each BP recording, two consecutive measurements need to be taken, at least 1 minute apart and with the person seated
- BP should be recorded twice daily, ideally in the morning and evening
- BP should be recorded for at least 4 days, ideally for 7 days
- discard the measurements taken on the first day and use the average value of all the remaining measurements

## Managing hypertension

ABPM/HBPM  $\geq$  135/85 mmHg (i.e. stage 1 hypertension)

- treat if  $< 80$  years of age and any of the following apply; target organ damage, established cardiovascular disease, renal disease, diabetes or a 10-year cardiovascular risk equivalent to 20% or greater

ABPM/HBPM  $\geq$  150/95 mmHg (i.e. stage 2 hypertension)

- offer drug treatment regardless of age

For patients  $< 40$  years consider specialist referral to exclude secondary causes.

### Step 1 treatment

- patients  $< 55$ -years-old: ACE inhibitor (A)
- patients  $> 55$ -years-old or of Afro-Caribbean origin: calcium channel blocker

### Step 2 treatment

- ACE inhibitor + calcium channel blocker (A + C)

### Step 3 treatment

- add a thiazide diuretic (D, i.e. A + C + D)

- NICE now advocate using either chlorthalidone (12.5-25.0 mg once daily) or indapamide (1.5 mg modified-release once daily or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide

NICE define a clinic BP  $\geq 140/90$  mmHg after step 3 treatment with optimal or best tolerated doses as resistant hypertension. They suggest step 4 treatment or seeking expert advice

#### Step 4 treatment

- consider further diuretic treatment
- if potassium  $< 4.5$  mmol/l add spironolactone 25mg od
- if potassium  $> 4.5$  mmol/l add higher-dose thiazide-like diuretic treatment
- if further diuretic therapy is not tolerated, or is contraindicated or ineffective, consider an alpha- or beta-blocker

If BP still not controlled seek specialist advice.

#### Blood pressure targets

	Clinic BP	ABPM / HBPM
Age $< 80$ years	140/90 mmHg	135/85 mmHg
Age $> 80$ years	150/90 mmHg	145/85 mmHg

#### New drugs

##### Direct renin inhibitors

- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs



Which one of the following agents is most useful in the maintenance of sinus rhythm in patients with atrial fibrillation?

- ☐ A. Verapamil
- ☐ B. Diltiazem
- ☐ C. Ibutilide
- ☐ D. Amiodarone
- ☐ E. Digoxin

[Next question](#)

### Atrial fibrillation: rate control and maintenance of sinus rhythm

The Royal College of Physicians and NICE published guidelines on the management of atrial fibrillation (AF) in 2006. The following is also based on the joint American Heart Association (AHA), American College of Cardiology (ACC) and European Society of Cardiology (ESC) 2012 guidelines

Agents used to control rate in patients with atrial fibrillation

- beta-blockers
- calcium channel blockers
- digoxin (not considered first-line anymore as they are less effective at controlling the heart rate during exercise. However, they are the preferred choice if the patient has coexistent heart failure)

Agents used to maintain sinus rhythm in patients with a history of atrial fibrillation

- sotalol
- amiodarone
- flecainide
- others (less commonly used in UK): disopyramide, dofetilide, procainamide, propafenone, quinidine

The table below indicates some of the factors which may be considered when considering either a rate control or rhythm control strategy

Factors favouring rate control	Factors favouring rhythm control
Older than 65 years History of ischaemic heart disease	Younger than 65 years Symptomatic First presentation Lone AF or AF secondary to a corrected precipitant (e.g. Alcohol) Congestive heart failure

Which one of the following non-invasive methods provides the most accurate assessment of whether a patient has coronary artery disease?

<input type="radio"/>	A. Contrast enhanced cardiac CT
<input type="radio"/>	B. Cardiac MRI with gadolinium
<input type="radio"/>	C. Exercise ECG
<input type="radio"/>	D. Cardiac SPECT with reversibility studies
<input type="radio"/>	E. Transoesophageal echocardiography

[Next question](#)

### Cardiac imaging: non-invasive techniques excluding echocardiography

The ability to image the heart using non-invasive techniques such as MRI, CT and radionuclides has evolved rapidly over recent years.

#### Nuclear imaging

These techniques use radiotracers which are extracted by normal myocardium. Examples include:

- thallium
- technetium (99mTc) sestamibi: a coordination complex of the radioisotope technetium-99m with the ligand methoxyisobutyl isonitrile (MIBI), used in 'MIBI' or cardiac Single Photon Emission Computed Tomography (SPECT) scans
- fluorodeoxyglucose (FDG): used in Positron Emission Tomography (PET) scans

The primary role of SPECT is to assess myocardial perfusion and myocardial viability. Two sets of images are usually acquired. First the myocardium at rest followed by images of the myocardium during stress (either exercise or following adenosine / dipyridamole). By comparing the rest with stress images any areas of ischaemia can be classified as reversible or fixed (e.g. Following a myocardial infarction). Cardiac PET is predominately a research tool at the current time

#### MUGA

- Multi Gated Acquisition Scan, also known as radionuclide angiography
- radionuclide (technetium-99m) is injected intravenously
- the patient is placed under a gamma camera
- may be performed as a stress test
- can accurately measure left ventricular ejection fraction. Typically used before and after cardiotoxic drugs are used

## **Cardiac Computed Tomography (CT)**

Cardiac CT is useful for assessing suspected ischaemic heart disease, using two main methods:

- calcium score: there is known to be a correlation between the amount of atherosclerotic plaque calcium and the risk of future ischaemic events. Cardiac CT can quantify the amount of calcium producing a 'calcium score'
- contrast enhanced CT: allows visualisation of the coronary artery lumen

If these two techniques are combined cardiac CT has a very high negative predictive value for ischaemic heart disease.

## **Cardiac MRI**

Cardiac MRI (commonly termed CMR) has become the gold standard for providing structural images of the heart. It is particularly useful when assessing congenital heart disease, determining right and left ventricular mass and differentiating forms of cardiomyopathy. Myocardial perfusion can also be assessed following the administration of gadolinium. Currently CMR provides limited data on the extent of coronary artery disease.

Please also see the British Heart Foundation link for an excellent summary.

Next

### Question 235 of 247

You review a 69-year-old man who is known to have angina and heart failure. His current medications include aspirin, simvastatin, bisoprolol, glyceryl trinitrate, ramipril and frusemide. Despite his current medications he is still having frequent angina attacks when he exerts himself. You decide to add a calcium channel blocker. Which one of the following is it most appropriate to add?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Felodipine |
| <input type="radio"/> | B. Diltiazem  |
| <input type="radio"/> | C. Nimodipine |
| <input type="radio"/> | D. Lacidipine |
| <input type="radio"/> | E. Verapamil  |

[Next question](#)

Verapamil and diltiazem should be avoided given his history of heart failure. Nimodipine and lacidipine are neither licensed nor used in patients with angina.

### Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery. NICE produced guidelines in 2011 covering the management of stable angina

#### Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- NICE recommend using either a beta-blocker or a calcium channel blocker first-line based on 'comorbidities, contraindications and the person's preference'
- if a calcium channel blocker is used as monotherapy a rate-limiting one such as verapamil or diltiazem should be used. If used in combination with a beta-blocker then use a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine). Remember that beta-blockers should not be prescribed concurrently with verapamil (risk of complete heart block)
- if there is a poor response to initial treatment then medication should be increased to the maximum tolerated dose (e.g. for atenolol 100mg od)
- if a patient is still symptomatic after monotherapy with a beta-blocker add a calcium channel blocker and vice versa
- if a patient is on monotherapy and cannot tolerate the addition of a calcium channel blocker or a beta-blocker then consider one of the following drugs: a long-acting nitrate, ivabradine, nicorandil or ranolazine
- if a patient is taking both a beta-blocker and a calcium-channel blocker then only add a third drug whilst a patient is awaiting assessment for PCI or CABG

#### Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy

- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

#### Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the  $I_f$  ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

Next

### Question 236 of 247

Which one of the following clinical signs would best indicate severe aortic stenosis?

<input type="radio"/>	A. Valvular gradient of less than 30 mmHg
<input type="radio"/>	B. Soft second heart sound
<input type="radio"/>	C. Quiet first heart sound
<input type="radio"/>	D. Development of an opening snap
<input type="radio"/>	E. Carotid radiation of ejection systolic murmur

[Next question](#)

Questions may sometimes refer to a soft A2 rather than a soft S2 (second heart sound), specifically mentioning the aortic component.

### Aortic stenosis

Features of severe aortic stenosis

- narrow pulse pressure
- slow rising pulse
- delayed ESM
- soft/absent S2
- S4
- thrill
- duration of murmur
- left ventricular hypertrophy or failure

Causes of aortic stenosis

- degenerative calcification (most common cause in older patients > 65 years)
- bicuspid aortic valve (most common cause in younger patients < 65 years)
- William's syndrome (supravalvular aortic stenosis)
- post-rheumatic disease
- subvalvular: HOCM

Management

- if asymptomatic then observe the patient is general rule
- if symptomatic then valve replacement
- if asymptomatic but valvular gradient > 50 mmHg and with features such as left ventricular systolic dysfunction then consider surgery
- balloon valvuloplasty is limited to patients with critical aortic stenosis who are not fit for valve replacement

You review a 60-year-old man who had a drug-eluting stent inserted 6 months ago for ischaemic heart disease. His current medication includes aspirin, clopidogrel, atorvastatin, ramipril and bisoprolol. He has developed an inguinal hernia and is keen for surgical repair. The cardiologists plan was to continue clopidogrel for 12 months following stent insertion. What is the most appropriate course of action?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Stop clopidogrel the day before the operation   |
| <input type="radio"/> | B. Stop clopidogrel 7 days before the operation  |
| <input type="radio"/> | C. Continue clopidogrel as normal  |
| <input type="radio"/> | D. Delay operation for 6 months  |
| <input type="radio"/> | E. Stop clopidogrel the day before the operation and start low-molecular weight heparin (prophylaxis dose) |

Next question

The AHA/ACC/SCAI/ACS/ADA published recommendations in 2007 stressed the importance of 12 months of dual antiplatelet therapy after placement of a drug-eluting stent (DES).

### Clopidogrel

Clopidogrel is an antiplatelet agent used in the management of cardiovascular disease. It was previously used when aspirin was not tolerated or contraindicated but there are now a number of conditions for which clopidogrel is used in addition to aspirin, for example in patients with an acute coronary syndrome. Following the 2010 NICE technology appraisal clopidogrel is also now first-line in patients following an ischaemic stroke and in patients with peripheral arterial disease.

#### Mechanism

- inhibits ADP binding to its platelet receptor

#### Interactions

- concurrent use of proton pump inhibitors (PPIs) may make clopidogrel less effective (MHRA July 2009)
- this advice was updated by the MHRA in April 2010, evidence seems inconsistent but omeprazole and esomeprazole still cause for concern. Other PPIs such as lansoprazole should be OK - please see the link for more details

A 55-year-old man is admitted with central chest pain. His ECG shows ST depression in the inferior leads and the chest pain requires intravenous morphine to settle. Past medical history includes a thrombolysed myocardial infarction 2 years ago, asthma and type 2 diabetes mellitus. Treatment with aspirin, clopidogrel and unfractionated heparin is commenced. Which one of the following factors should determine if an intravenous glycoprotein IIb/IIIa receptor antagonist is to be given?

- ☐ A. High GRACE (Global Registry of Acute Cardiac Events) risk score + whether a percutaneous coronary intervention is to be performed
- ☐ B. Degree of ST depression
- ☐ C. High GRACE (Global Registry of Acute Cardiac Events) risk score
- ☐ D. Presence of a left ventricular thrombus
- ☐ E. The presence of recurrent cardiac chest pain

### Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive

- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

**Antithrombin** treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patient's creatinine is  $> 265 \mu\text{mol/l}$  unfractionated heparin should be given.

**Clopidogrel** 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

**Coronary angiography** should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.



The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

<b>Aspirin</b>	Antiplatelet - inhibits the production of thromboxane A <sub>2</sub>
<b>Clopidogrel</b>	Antiplatelet - inhibits ADP binding to its platelet receptor
<b>Enoxaparin</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Fondaparinux</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Bivalirudin</b>	Reversible direct thrombin inhibitor

Next

### Question 239 of 247

A 13-year-old girl presents with palpitations, fatigue and dyspnoea. She has had symptoms for around a year. There is no history of syncope or chest pain. On examination she has a pan-systolic murmur associated with giant V waves in the jugular venous pulse. Auscultation of the chest is unremarkable. A resting ECG is normal but a 24 hour tape shows a short burst of supraventricular tachycardia. What is the most likely diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Atrial septal defect                            |
| <input type="radio"/> | B. Pulmonary stenosis                              |
| <input type="radio"/> | C. Hypertrophic obstructive cardiomyopathy         |
| <input type="radio"/> | D. Arrhythmogenic right ventricular cardiomyopathy |
| <input type="radio"/> | E. Ebstein's anomaly                               |

[Next question](#)

### Ebstein's anomaly

Ebstein's anomaly is a congenital heart defect characterised by low insertion of the tricuspid valve resulting in a large atrium and small ventricle. It is sometimes referred to as 'atrialisation' of the right ventricle.

#### Associations

- tricuspid incompetence (pan-systolic murmur, giant V waves in JVP)
- Wolff-Parkinson White syndrome

Ebstein's anomaly may be caused by exposure to lithium in-utero

[Next](#)

### Question 240 of 247

You review a 24-year-old woman who has recently been diagnosed as having long QT syndrome type I (LQTS1). You are discussing the need to avoid certain drugs and other aggravating factors. Which one of the following should be avoided if possible?

- ☐ A. Methotrexate
- ☐ B. Sertraline
- ☐ C. Grapefruit juice
- ☐ D. Carbamazepine
- ☐ E. Doxycycline

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"><li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li><li>Romano-Ward syndrome (no deafness)</li></ul>	<ul style="list-style-type: none"><li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li><li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li><li>methadone</li><li>chloroquine</li><li>terfenadine**</li><li>erythromycin</li></ul>	<ul style="list-style-type: none"><li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li><li>acute myocardial infarction</li><li>myocarditis</li><li>hypothermia</li><li>subarachnoid haemorrhage</li></ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

### Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

Next

### Question 241 of 247

You review an 82-year-old woman in clinic. Last month she had a one-off blood pressure reading of 150/92 mmHg and was offered ambulatory blood pressure monitoring. This shows an average reading of 146/94 mmHg. She has no significant past medical history of note other than hypothyroidism. Her 10-year cardiovascular risk is calculated to be 16%. What is the most appropriate management?

- ☐ A. Arrange further ambulatory blood pressure monitoring
- ☐ B. Start a thiazide-type diuretic
- ☐ C. Give lifestyle advice and repeat blood pressure in 6 months
- ☐ D. Start an ACE inhibitor
- ☐ E. Start a calcium channel blocker

[Next question](#)

NICE now only recommend diagnosing people over the age of 80 years as hypertensive if they have stage 2 hypertension (ABPM daytime average or HBPM average BP  $\geq$  150/95 mmHg). Remember that the diagnostic criteria are different from the blood pressure targets once treatment has started, which for people over the age of 80 years are:

- clinic readings  $<$  150/90 mmHg
- ABPM/HBPM  $<$  145/85 mmHg

### Hypertension: diagnosis and management

NICE published updated guidelines for the management of hypertension in 2011. Some of the key changes include:

- classifying hypertension into stages
- recommending the use of ambulatory blood pressure monitoring (ABPM) and home blood pressure monitoring (HBPM)
- calcium channel blockers are now considered superior to thiazides
- bendroflumethiazide is no longer the thiazide of choice

### Blood pressure classification

This becomes relevant later in some of the management decisions that NICE advocate.

<b>Stage 1 hypertension</b>	Clinic BP $\geq$ 140/90 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 135/85 mmHg
<b>Stage 2 hypertension</b>	Clinic BP $\geq$ 160/100 mmHg and subsequent ABPM daytime average or HBPM average BP $\geq$ 150/95 mmHg
<b>Severe hypertension</b>	Clinic systolic BP $\geq$ 180 mmHg, or clinic diastolic BP $\geq$ 110 mmHg

### Diagnosing hypertension

If a BP reading is  $\geq 140 / 90$  mmHg patients should be offered ABPM to confirm the diagnosis.

Patients with a BP reading of  $\geq 180/110$  mmHg should be considered for immediate treatment.

Ambulatory blood pressure monitoring (ABPM)

- at least 2 measurements per hour during the person's usual waking hours (for example, between 08:00 and 22:00)
- use the average value of at least 14 measurements

If ABPM is not tolerated or declined HBPM should be offered.

Home blood pressure monitoring (HBPM)

- for each BP recording, two consecutive measurements need to be taken, at least 1 minute apart and with the person seated
- BP should be recorded twice daily, ideally in the morning and evening
- BP should be recorded for at least 4 days, ideally for 7 days
- discard the measurements taken on the first day and use the average value of all the remaining measurements

## Managing hypertension

ABPM/HBPM  $\geq 135/85$  mmHg (i.e. stage 1 hypertension)

- treat if  $< 80$  years of age and any of the following apply; target organ damage, established cardiovascular disease, renal disease, diabetes or a 10-year cardiovascular risk equivalent to 20% or greater

ABPM/HBPM  $\geq 150/95$  mmHg (i.e. stage 2 hypertension)

- offer drug treatment regardless of age

For patients  $< 40$  years consider specialist referral to exclude secondary causes.

Step 1 treatment

- patients  $< 55$ -years-old: ACE inhibitor (A)
- patients  $> 55$ -years-old or of Afro-Caribbean origin: calcium channel blocker

Step 2 treatment

- ACE inhibitor + calcium channel blocker (A + C)

Step 3 treatment

- add a thiazide diuretic (D, i.e. A + C + D)

- NICE now advocate using either chlorthalidone (12.5-25.0 mg once daily) or indapamide (1.5 mg modified-release once daily or 2.5 mg once daily) in preference to a conventional thiazide diuretic such as bendroflumethiazide

NICE define a clinic BP  $\geq 140/90$  mmHg after step 3 treatment with optimal or best tolerated doses as resistant hypertension. They suggest step 4 treatment or seeking expert advice

#### Step 4 treatment

- consider further diuretic treatment
- if potassium  $< 4.5$  mmol/l add spironolactone 25mg od
- if potassium  $> 4.5$  mmol/l add higher-dose thiazide-like diuretic treatment
- if further diuretic therapy is not tolerated, or is contraindicated or ineffective, consider an alpha- or beta-blocker

If BP still not controlled seek specialist advice.

#### Blood pressure targets

	Clinic BP	ABPM / HBPM
Age $< 80$ years	140/90 mmHg	135/85 mmHg
Age $> 80$ years	150/90 mmHg	145/85 mmHg

#### New drugs

##### Direct renin inhibitors

- e.g. Aliskiren (branded as Rasilez)
- by inhibiting renin blocks the conversion of angiotensinogen to angiotensin I
- no trials have looked at mortality data yet. Trials have only investigated fall in blood pressure. Initial trials suggest aliskiren reduces blood pressure to a similar extent as angiotensin converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists
- adverse effects were uncommon in trials although diarrhoea was occasionally seen
- only current role would seem to be in patients who are intolerant of more established antihypertensive drugs

### Question 242 of 247

What is the target INR for a patient with a mechanical mitral valve?

- ☐ A. 4.0-4.5
- ☐ B. 4.0
- ☐ C. 3.0-4.0
- ☐ D. 2.5-3.5
- ☐ E. 2.0-3.0

[Next question](#)

Mechanical valves - target INR:

- aortic: 2.0-3.0
- mitral: 2.5-3.5

### Prosthetic heart valves

The most common valves which need replacing are the aortic and mitral valve. There are two main options for replacement: biological (bioprosthetic) or mechanical.

Biological (bioprosthetic) valves	Mechanical valves
Usually bovine or porcine in origin	The most common type now implanted is the bileaflet valve. Ball-and-cage valves are rarely used nowadays
Major disadvantage is structural deterioration and calcification over time. Most older patients (> 65 years for aortic valves and > 70 years for mitral valves) receive a bioprosthetic valve	Mechanical valves have a low failure rate
Long-term anticoagulation not usually needed. Warfarin may be given for the first 3 months depending on patient factors. Low-dose aspirin is given long-term.	Major disadvantage is the increased risk of thrombosis meaning long-term anticoagulation is needed. Aspirin is normally given in addition unless there is a contraindication.
	Target INR <ul style="list-style-type: none"><li>• aortic: 2.0-3.0</li><li>• mitral: 2.5-3.5</li></ul>

Following the 2008 NICE guidelines for prophylaxis of endocarditis antibiotics are no longer recommended for common procedures such as dental work.



What is the main reason for checking the urea and electrolytes prior to commencing a patient on amiodarone?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. To detect hyponatraemia           |
| <input type="radio"/> | B. To detect impaired renal function |
| <input type="radio"/> | C. To detect a metabolic acidosis    |
| <input type="radio"/> | D. To detect hyperkalaemia           |
| <input type="radio"/> | E. To detect hypokalaemia            |

Next question

All antiarrhythmic drugs have the potential to cause arrhythmias. Coexistent hypokalaemia significantly increases this risk.

### Amiodarone

Amiodarone is a class III antiarrhythmic agent used in the treatment of atrial, nodal and ventricular tachycardias. The main mechanism of action is by blocking potassium channels which inhibits repolarisation and hence prolongs the action potential. Amiodarone also has other actions such as blocking sodium channels (a class I effect)

The use of amiodarone is limited by a number of factors

- long half-life (20-100 days)
- should ideally be given into central veins (causes thrombophlebitis)
- has proarrhythmic effects due to lengthening of the QT interval
- interacts with drugs commonly used concurrently e.g. Decreases metabolism of warfarin
- numerous long-term adverse effects (see below)

Monitoring of patients taking amiodarone

- TFT, LFT, U&E, CXR prior to treatment
- TFT, LFT every 6 months

Adverse effects of amiodarone use

- thyroid dysfunction
- corneal deposits
- pulmonary fibrosis/pneumonitis
- liver fibrosis/hepatitis
- peripheral neuropathy, myopathy
- photosensitivity
- 'slate-grey' appearance
- thrombophlebitis and injection site reactions
- bradycardia

Which one of the following statements regarding Brugada syndrome is correct?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Usually inherited as an autosomal recessive disease |
| <input type="radio"/> | B. Is associated with left bundle branch block         |
| <input type="radio"/> | C. Most common presentation is dilated cardiomyopathy  |
| <input type="radio"/> | D. Management is with beta-blockers                    |
| <input type="radio"/> | E. More common in Asians                               |

Next question

### Brugada syndrome

Brugada syndrome is a form of inherited cardiovascular disease with may present with sudden cardiac death. It is inherited in an autosomal dominant fashion and has an estimated prevalence of 1:5,000-10,000. Brugada syndrome is more common in Asians.

#### Pathophysiology

- a large number of variants exist
- around 20-40% of cases are caused by a mutation in the SCN5A gene which encodes the myocardial sodium ion channel protein

#### ECG changes

- convex ST elevation V1-V3
- partial right bundle branch block
- changes may be more apparent following flecainide

#### Management

- implantable cardioverter-defibrillator

A 62-year-old female with no past medical history is admitted to hospital with a left-sided hemiparesis. Examination reveals that she is in atrial fibrillation. CT scan of her brain shows a cerebral infarction. What is the most appropriate anticoagulation strategy for this patient?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Life-long warfarin, started immediately                                   |
| <input type="radio"/> | B. Aspirin started immediately switching to life-long warfarin after 2 weeks |
| <input type="radio"/> | C. Life-long aspirin, started immediately                                    |
| <input type="radio"/> | D. Life-long aspirin started after 2 weeks                                   |
| <input type="radio"/> | E. 6 months of warfarin, started immediately                                 |

[Next question](#)

### Atrial fibrillation: post-stroke

NICE issued guidelines on atrial fibrillation (AF) in 2006. They included advice on the management of patients with AF who develop a stroke or transient-ischaemic attack (TIA).

Recommendations include:

- following a stroke or TIA warfarin should be given as the anticoagulant of choice. Aspirin/dipyridamole should only be given if needed for the treatment of other comorbidities
- in acute stroke patients, in the absence of haemorrhage, anticoagulation therapy should be commenced after 2 weeks. If imaging shows a very large cerebral infarction then the initiation of anticoagulation should be delayed

**Question 246 of 247**

Next

A 62-year-old man is examined in the cardiology clinic. During cardiac auscultation it is noted that the pulmonary component of the second heart sound occurs before the aortic. Which one of the following is associated with this finding?

<input type="radio"/>	A. Pulmonary stenosis
<input type="radio"/>	B. Left bundle branch block
<input type="radio"/>	C. Right bundle branch block
<input type="radio"/>	D. Atrial septal defect
<input type="radio"/>	E. Deep inspiration

Next question

**Second heart sound (S2)**

- loud: hypertension
- soft: AS
- fixed split: ASD
- reversed split: LBBB

Left bundle branch block causes a reversed split second heart sound. Atrial septal defects cause fixed splitting of S2

**Heart sounds: S2**

S2 is caused by the closure of the aortic valve (A2) closely followed by that of the pulmonary valve (P2)

Causes of a loud S2

- hypertension: systemic (loud A2) or pulmonary (loud P2)
- hyperdynamic states
- atrial septal defect without pulmonary hypertension

Causes of a soft S2

- aortic stenosis

Causes of fixed split S2

- atrial septal defect

Causes of a widely split S2

- deep inspiration
- RBBB

- pulmonary stenosis
- severe mitral regurgitation

Causes of a reversed (paradoxical) split S2 (P2 occurs before A2)

- LBBB
- severe aortic stenosis
- right ventricular pacing
- WPW type B (causes early P2)
- patent ductus arteriosus

### Question 247 of 247

A 45-year-old man presents with fever. On examination he is noted to have a pan-systolic murmur and splinter haemorrhages. He is generally unwell with a blood pressure of 100/60 mmHg and a temperature of 38.8°C. What is the most suitable antibiotic therapy until blood culture results are known?

<input type="radio"/>	A. IV flucloxacillin + gentamicin
<input type="radio"/>	B. IV benzylpenicillin + gentamicin
<input type="radio"/>	C. IV vancomycin + gentamicin
<input type="radio"/>	D. IV vancomycin + benzylpenicillin
<input type="radio"/>	E. IV ceftriaxone + benzylpenicillin

### Infective endocarditis: prognosis and management

Poor prognostic factors

- Staph aureus infection (see below)
- prosthetic valve (especially 'early', acquired during surgery)
- culture negative endocarditis
- low complement levels

Mortality according to organism

- staphylococci - 30%
- bowel organisms - 15%
- streptococci - 5%

Current antibiotic guidelines (source: British National Formulary)

Scenario	Suggested antibiotic therapy
Initial blind therapy	Flucloxacillin + gentamicin (benzylpenicillin + gentamicin if symptoms less severe)
Initial blind therapy if prosthetic valve is present or patient is penicillin allergic	Vancomycin + rifampicin + gentamicin
Endocarditis caused by staphylococci	Flucloxacillin (add rifampicin if prosthetic valve, vancomycin + rifampicin if penicillin allergic or MRSA)
Native valve endocarditis caused by fully-sensitive streptococci (e.g. viridans)	Benzylpenicillin (large vegetation, intracardial abscess or infected emboli then benzylpenicillin + gentamicin, vancomycin if penicillin allergic)
Native valve endocarditis caused by less sensitive streptococci OR prosthetic valve endocarditis caused by streptococci	Benzylpenicillin + gentamicin (vancomycin + gentamicin if penicillin allergic)

## Indications for surgery

- severe valvular incompetence
- aortic abscess (often indicated by a lengthening PR interval)
- infections resistant to antibiotics/fungal infections
- cardiac failure refractory to standard medical treatment
- recurrent emboli after antibiotic therapy

**Question 1 of 134**

Next

A 27-year-old woman is reviewed in the asthma clinic. She currently uses salbutamol inhaler 100mcg prn combined with beclometasone dipropionate inhaler 400mcg bd. Despite this she is having frequent exacerbations of her asthma and recently required a course of prednisolone. What is the most appropriate next step in management?

- ☐ A. Add a leukotriene receptor antagonist
- ☐ B. Add tiotropium
- ☐ C. Add salmeterol
- ☐ D. Start to take the salbutamol regularly, 2 puffs qds
- ☐ E. Switch beclometasone to fluticasone

Next question

**Asthma: stepwise management in adults**

The management of stable asthma is now well established with a step-wise approach:

<b>Step 1</b>	Inhaled short-acting B2 agonist as required
<b>Step 2</b>	Add inhaled steroid at 200-800 mcg/day*  400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
<b>Step 3</b>	1. Add inhaled long-acting B2 agonist (LABA)  2. Assess control of asthma: <ul style="list-style-type: none"> <li>• good response to LABA - continue LABA</li> <li>• benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose)</li> <li>• no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline</li> </ul>
<b>Step 4</b>	Consider trials of: <ul style="list-style-type: none"> <li>• increasing inhaled steroid up to 2000 mcg/day*</li> <li>• addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet</li> </ul>
<b>Step 5</b>	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets  Maintain high dose inhaled steroid at 2000 mcg/day*  Refer patient for specialist care

\*beclometasone dipropionate or equivalent



## Additional notes

### Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone

Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles

Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

**Question 2 of 134**

Next

Which one of the following would cause a rise in the carbon monoxide transfer factor (TLCO)?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Emphysema             |
| <input type="radio"/> | B. Pulmonary embolism    |
| <input type="radio"/> | C. Pulmonary haemorrhage |
| <input type="radio"/> | D. Pneumonia             |
| <input type="radio"/> | E. Pulmonary fibrosis    |

Next question

**Transfer factor**

- raised: asthma, haemorrhage, left-to-right shunts, polycythaemia
- low: everything else

Where alveolar haemorrhage occurs the TLCO tends to increase due to the enhanced uptake of carbon monoxide by intra-alveolar haemoglobin

**Transfer factor**

The transfer factor describes the rate at which a gas will diffuse from alveoli into blood. Carbon monoxide is used to test the rate of diffusion. Results may be given as the total gas transfer (TLCO) or that corrected for lung volume (transfer coefficient, KCO)

Causes of a raised TLCO	Causes of a lower TLCO
<ul style="list-style-type: none"> <li>• asthma</li> <li>• pulmonary haemorrhage (Wegener's, Goodpasture's)</li> <li>• left-to-right cardiac shunts</li> <li>• polycythaemia</li> <li>• hyperkinetic states</li> <li>• male gender, exercise</li> </ul>	<ul style="list-style-type: none"> <li>• pulmonary fibrosis</li> <li>• pneumonia</li> <li>• pulmonary emboli</li> <li>• pulmonary oedema</li> <li>• emphysema</li> <li>• anaemia</li> <li>• low cardiac output</li> </ul>

KCO also tends to increase with age. Some conditions may cause an increased KCO with a normal or reduced TLCO

- pneumonectomy/lobectomy
- scoliosis/kyphosis
- neuromuscular weakness
- ankylosis of costovertebral joints e.g. ankylosing spondylitis

### Question 3 of 134

Next

Which one of the following is responsible for farmer's lung?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. <i>Aspergillus clavatus</i>           |
| <input type="radio"/> | B. <i>Saccharopolyspora rectivirgula</i> |
| <input type="radio"/> | C. <i>Candida albicans</i>               |
| <input type="radio"/> | D. <i>Mycobacterium avium</i>            |
| <input type="radio"/> | E. <i>Avian proteins</i>                 |

Next question

*Saccharopolyspora rectivirgula* causes farmer's lung, a type of EAA

### Extrinsic allergic alveolitis

Extrinsic allergic alveolitis (EAA, also known as hypersensitivity pneumonitis) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles. It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase.

#### Examples

- bird fanciers' lung: avian proteins
- farmers lung: spores of *Saccharopolyspora rectivirgula* (formerly *Micropolyspora faeni*)
- malt workers' lung: *Aspergillus clavatus*
- mushroom workers' lung: thermophilic actinomycetes\*

#### Presentation

- acute: occur 4-8 hrs after exposure, SOB, dry cough, fever
- chronic

#### Investigation

- chest x-ray: upper lobe fibrosis
- bronchoalveolar lavage: lymphocytosis
- blood: NO eosinophilia

\*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as *Micropolyspora faeni*

**Question 4 of 134**

Next

Which of the following factors is least useful in assessing patients with a poor prognosis in community-acquired pneumonia?

<input type="radio"/>	A. Mini-mental score of 6/10
<input type="radio"/>	B. Urea of 11.4 mmol/l
<input type="radio"/>	C. C-reactive protein of 154
<input type="radio"/>	D. Respiratory rate of 30
<input type="radio"/>	E. Aged 75 years old

Next question

The C-reactive protein is the least useful of the above in predicting mortality in patients with community-acquired pneumonia. The rest of the answers are part of the CURB-65 criteria

**Pneumonia: prognostic factors**

CURB-65 criteria of severe pneumonia

- Confusion (abbreviated mental test score  $\leq 8/10$ )
- Urea  $> 7$  mmol/L
- Respiratory rate  $\geq 30$  / min
- BP: systolic  $\leq 90$  or diastolic  $\leq 60$  mmHg
- age  $\geq 65$  years

Patients with 3 or more (out of 5) of the above criteria are regarded as having a severe pneumonia

Other factors associated with a poor prognosis include:

- presence of coexisting disease
- hypoxaemia ( $pO_2 < 8$  kPa) independent of  $FiO_2$

**Question 5 of 134**

Next

A 24-year-old female presents with episodic wheezing and shortness of breath for the past 4 months. She has smoked for the past 8 years and has a history of eczema. Examination of her chest is unremarkable. Spirometry is arranged and is reported as normal. What is the most appropriate management of her symptoms?

- ☐ A. Peak flow diary
- ☐ B. Trial of lansoprazole
- ☐ C. Baseline FEV1 repeated following inhaled corticosteroids
- ☐ D. Arrange a chest x-ray
- ☐ E. Trial of salbutamol inhaler

Next question

Asthma diagnosis - if high probability of asthma - start treatment

The new British Thoracic Society guidelines take a more practical approach to diagnosing asthma. If a patient has typical symptoms of asthma a trial of treatment is recommended. Normal spirometry when the patient is well does not exclude a diagnosis of asthma. The smoking history is unlikely to be relevant at her age.

What is not necessarily clear is whether all patients should have spirometry prior to starting treatment - how do you interpret the guidelines?

**Asthma: diagnosis in adults**

The 2008 British Thoracic Society guidelines marked a subtle change in the approach to diagnosing asthma. This approach is supported in the updated 2011 guidelines. It suggests dividing patients into a high, intermediate and low probability of having asthma based on the presence or absence of typical symptoms. A list can be found in the external link but include typical symptoms such as wheeze, nocturnal cough etc

Example of features used to assess asthma (not complete, please see link)

Increase possibility of asthma	Decrease possibility of asthma
<ul style="list-style-type: none"><li>• Wheeze, breathlessness, chest tightness and cough, worse at night/early morning</li><li>• History of atopic disorder</li><li>• Wheeze heard on auscultation</li><li>• Unexplained peripheral blood eosinophilia</li></ul>	<ul style="list-style-type: none"><li>• Prominent dizziness, light-headedness, peripheral tingling</li><li>• Chronic productive cough in the absence of wheeze or breathlessness</li><li>• Repeatedly normal physical examination</li><li>• Significant smoking history (i.e. &gt; 20 pack-years)</li><li>• Normal PEF or spirometry when symptomatic</li></ul>

Management is based on this assessment:

- high probability: trial of treatment
- intermediate probability: see below
- low probability: investigate/treat other condition

For patients with an intermediate probability of asthma further investigations are suggested. The guidelines state that spirometry is the preferred initial test:

- FEV1/FVC < 0.7: trial of treatment
- FEV1/FVC > 0.7: further investigation/consider referral

Recent studies have shown the limited value of other 'objective' tests. It is now recognised that in patients with normal or near-normal pre-treatment lung function there is little room for measurable improvement in FEV1 or peak flow.

A > 400 ml improvement in FEV1 is considered significant

- before and after 400 mcg inhaled salbutamol in patients with diagnostic uncertainty and airflow obstruction present at the time of assessment
- if there is an incomplete response to inhaled salbutamol, after either inhaled corticosteroids (200 mcg twice daily beclometasone equivalent for 6-8 weeks) or oral prednisolone (30 mg once daily for 14 days)

It is now advised to interpret peak flow variability with caution due to the poor sensitivity of the test

- diurnal variation % =  $[(\text{Highest} - \text{Lowest PEFr}) / \text{Highest PEFr}] \times 100$
- assessment should be made over 2 weeks
- greater than 20% diurnal variation is considered significant

Which one of the following is a contraindication to surgical resection in lung cancer?

<input type="radio"/>	A. Haemoptysis
<input type="radio"/>	B. FEV 1.9 litres
<input type="radio"/>	C. Histology shows squamous cell cancer
<input type="radio"/>	D. Vocal cord paralysis
<input type="radio"/>	E. Calcium = 2.84 mmol/L

Next question

Contraindications to lung cancer surgery include SVC obstruction, FEV < 1.5, MALIGNANT pleural effusion, and vocal cord paralysis

Paralysis of a vocal cord implies extracapsular spread to mediastinal nodes and is an indication of inoperability.

### Lung cancer: non-small cell management

#### Management

- only 20% suitable for surgery
- mediastinoscopy performed prior to surgery as CT does not always show mediastinal lymph node involvement
- curative or palliative radiotherapy
- poor response to chemotherapy

#### Surgery contraindications

- assess general health
- stage IIIb or IV (i.e. metastases present)
- FEV1 < 1.5 litres is considered a general cut-off point\*
- malignant pleural effusion
- tumour near hilum
- vocal cord paralysis
- SVC obstruction

\* However if FEV1 < 1.5 for lobectomy or < 2.0 for pneumonectomy then some authorities advocate further lung function tests as operations may still go ahead based on the results

**Question 7 of 134**

Next

A 52-year-old man with a history of alcohol dependence is admitted with fever and feeling generally unwell. An admission chest x-ray shows consolidation in the right upper lobe with early cavitation. What is the most likely causative organism?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. <i>Streptococcus pneumoniae</i> |
| <input type="radio"/> | B. <i>Legionella pneumophila</i>   |
| <input type="radio"/> | C. <i>Staphylococcus aureus</i>    |
| <input type="radio"/> | D. <i>Klebsiella pneumoniae</i>    |
| <input type="radio"/> | E. <i>Mycoplasma pneumoniae</i>    |

Next question

Pneumonia in an alcoholic - Klebsiella

**Pneumonia: community-acquired**

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- *Staphylococcus aureus*: commonly after the 'flu
- atypical pneumonias (e.g. Due to *Mycoplasma pneumoniae*)
- viruses

*Klebsiella pneumoniae* is classically in alcoholics

***Streptococcus pneumoniae* (pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

**Management**

low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital

- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin



**Question 8 of 134**

Next

A 74-year-old woman with thyroid cancer is admitted due to shortness of breath. What is the best investigation to assess for possible compression of the upper airways?

<input type="radio"/>	A. Arterial blood gases
<input type="radio"/>	B. Forced vital capacity
<input type="radio"/>	C. Transfer factor
<input type="radio"/>	D. Peak expiratory flow rate
<input type="radio"/>	E. Flow volume loop

Next question

Flow volume loop is the investigation of choice for upper airway compression

**Flow volume loop**

A normal flow volume loop is often described as a 'triangle on top of a semi circle'

Flow volume loops are the most suitable way of assessing compression of the upper airway

You review a 26-year-old woman. She has a history of asthma and is prescribed salbutamol 100mcg 2 puffs prn, beclometasone dipropionate 400mcg bd and salmeterol 50mcg bd. Last week she found out she was pregnant and stopped the beclometasone and salmeterol inhalers as she was concerned about potential harm to the pregnancy. What is the most appropriate action?

- ☐ A. Reduce beclometasone to 200mcg bd and continue salmeterol at the same dose
- ☐ B. Stop beclometasone and salmeterol inhalers + refer to a respiratory physician
- ☐ C. Reduce beclometasone to 200mcg bd and stop salmeterol
- ☐ D. Restart beclomethasone at same dose and stop salmeterol
- ☐ E. Reassure + restart beclometasone and salmeterol inhalers

Next question

Both the BNF and British Thoracic Society guidelines stress the need for good control of asthma during pregnancy. The BNF advises that 'inhaled drugs, theophylline and prednisolone can be taken as normal during pregnancy and breast-feeding'.

### Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

<b>Step 1</b>	Inhaled short-acting B2 agonist as required
<b>Step 2</b>	Add inhaled steroid at 200-800 mcg/day*  400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
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\*beclometasone dipropionate or equivalent

## **Additional notes**

Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
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Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles

Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

Which one of the following causes of lung fibrosis predominately affect the upper zones?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Bleomycin                       |
| <input type="radio"/> | B. Rheumatoid arthritis            |
| <input type="radio"/> | C. Cryptogenic fibrosis alveolitis |
| <input type="radio"/> | D. Methotrexate                    |
| <input type="radio"/> | E. Extrinsic allergic alveolitis   |

Next question

### Lung fibrosis

It is important in the exam to be able to differentiate between conditions causing predominately upper or lower zone fibrosis. It should be noted that the more common causes (cryptogenic fibrosing alveolitis, drugs) tend to affect the lower zones

Fibrosis predominately affecting the upper zones

- extrinsic allergic alveolitis
- coal worker's pneumoconiosis/progressive massive fibrosis
- silicosis
- sarcoidosis
- ankylosing spondylitis (rare)
- histiocytosis
- tuberculosis

Fibrosis predominately affecting the lower zones

- cryptogenic fibrosing alveolitis
- most connective tissue disorders (except ankylosing spondylitis)
- drug-induced: amiodarone, bleomycin, methotrexate
- asbestosis

A chest x-ray of a patient with sarcoidosis shows bilateral hilar lymphadenopathy but is otherwise normal. What chest x-ray stage does this correspond to?

<input type="radio"/>	A. Stage 0
<input type="radio"/>	B. Stage 1
<input type="radio"/>	C. Stage 2
<input type="radio"/>	D. Stage 3
<input type="radio"/>	E. Stage 4

[Next question](#)

#### Sarcoidosis CXR

- 1 = BHL
- 2 = BHL + infiltrates
- 3 = infiltrates
- 4 = fibrosis

#### Sarcoidosis: investigation

There is no one diagnostic test for sarcoidosis and hence diagnosis is still largely clinical. ACE levels have a sensitivity of 60% and specificity of 70% and are therefore not reliable in the diagnosis of sarcoidosis although they may have a role in monitoring disease activity. Routine bloods may show hypercalcaemia (seen in 10% of patients) and a raised ESR

A chest x-ray may show the following changes:

- stage 0 = normal
- stage 1 = bilateral hilar lymphadenopathy (BHL)
- stage 2 = BHL + interstitial infiltrates
- stage 3 = diffuse interstitial infiltrates only
- stage 4 = diffuse fibrosis

Other investigations\*

- spirometry: may show a restrictive defect
- tissue biopsy: non-caseating granulomas
- gallium-67 scan - not used routinely

\*the Kveim test (where part of the spleen from a patient with known sarcoidosis is injected under the skin) is no longer performed due to concerns about cross-infection

A 45-year-old female develops pleuritic chest pain following a hysterectomy 10 days ago. Low-molecular weight heparin is given initially and CTPA confirms a pulmonary embolism. There is no previous history of venous thromboembolism. How long should the patient be warfarinised for?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Not suitable for anticoagulation |
| <input type="radio"/> | B. At least 4 weeks                 |
| <input type="radio"/> | C. At least 3 months                |
| <input type="radio"/> | D. At least 6 months                |
| <input type="radio"/> | E. 12 months                        |

[Next question](#)

As this patient has a temporary risk factor for a thromboembolic event the recommended period of anticoagulation is 3 months.

### Pulmonary embolism: management

The NICE guidelines of 2012 provided some clarity on how long patients should be anticoagulated for after a pulmonary embolism (PE). Selected points are listed below.

Low molecular weight heparin (LMWH) or fondaparinux should be given initially after a PE is diagnosed. An exception to this is for patients with a massive PE where thrombolysis is being considered. In such a situation unfractionated heparin should be used.

- a vitamin K antagonist (i.e. warfarin) should be given within 24 hours of the diagnosis
- the LMWH or fondaparinux should be continued for at least 5 days or until the international normalised ratio (INR) is 2.0 or above for at least 24 hours, whichever is longer, i.e. LMWH or fondaparinux is given at the same time as warfarin until the INR is in the therapeutic range
- warfarin should be continued for at least 3 months. At 3 months, NICE advise that clinicians should 'assess the risks and benefits of extending treatment'
- NICE advise extending warfarin beyond 3 months for patients with *unprovoked* PE. This essentially means that if there was no obvious cause or provoking factor (surgery, trauma, significant immobility) it may imply the patient has a tendency to thrombosis and should be given treatment longer than the norm of 3 months
- for patients with active cancer NICE recommend using LMWH for 6 months

### Thrombolysis

- thrombolysis is now recommended as the first-line treatment for massive PE where there is circulatory failure (e.g. hypotension). Other invasive approaches should be considered where appropriate facilities exist

**Question 13 of 134**

Next

A 69-year-old man with chronic obstructive pulmonary disease (COPD) presents to the Emergency Department with dyspnoea. Three days ago he was started on amoxicillin and prednisolone by his GP. Since arriving in the department he has been given back-to-back nebulised salbutamol and ipratropium bromide. The oxygen concentration has been titrated to 28% to achieve a saturation of 88-92%. Due to his poor response to treatment an aminophylline infusion is started. Thirty minutes later, his arterial blood gases show the following (taken on 28% oxygen):

pH	7.30
pCO <sub>2</sub>	7.6 kPa
pO <sub>2</sub>	8.1 kPa

What is the most appropriate next step in management?

- ☐ A. Intravenous magnesium sulphate
- ☐ B. Intravenous hydrocortisone
- ☐ C. Decrease his oxygen to 24%
- ☒ D. Non-invasive ventilation
- ☐ E. Increase his oxygen to 35%

Intravenous magnesium sulphate is useful in acute asthma, rather than COPD. Giving intravenous hydrocortisone is unlikely to make any difference given that he has had three days worth of prednisolone already.

**Non-invasive ventilation**

The British Thoracic Society (BTS) published guidelines in 2002 on the use of non-invasive ventilation in acute respiratory failure. Following these the Royal College of Physicians published guidelines in 2008.

Non-invasive ventilation - key indications

- COPD with respiratory acidosis pH 7.25-7.35
- type II respiratory failure secondary to chest wall deformity, neuromuscular disease or obstructive sleep apnoea
- cardiogenic pulmonary oedema unresponsive to CPAP
- weaning from tracheal intubation

Recommended initial settings for bi-level pressure support in COPD

- Expiratory Positive Airway Pressure (EPAP): 4-5 cm H<sub>2</sub>O
- Inspiratory Positive Airway Pressure (IPAP): RCP advocate 10 cm H<sub>2</sub>O whilst BTS suggest 12-15 cm H<sub>2</sub>O
- back up rate: 15 breaths/min
- back up inspiration:expiration ratio: 1:3

**Question 14 of 134**

Next

A 65-year-old female with a history of chronic obstructive pulmonary disease (COPD) is reviewed in the Emergency Department. She has presented with a sudden worsening of her dyspnoea associated with haemoptysis. What is the most suitable initial imaging investigation to exclude a pulmonary embolism?

- ☐ A. Ventilation-perfusion scan
- ☐ B. Echocardiogram
- ☐ C. Pulmonary angiography
- ☐ D. Computed tomographic pulmonary angiography
- ☐ E. MRI thorax

Next question

Pulmonary embolism - CTPA is first-line investigation

It is still common in UK hospitals, despite guidelines, for a ventilation-perfusion scan to be done first-line

**Pulmonary embolism: investigation****2012 NICE guidelines**

All patients with symptoms or signs suggestive of a PE should have a history taken, examination performed and a chest x-ray to exclude other pathology.

If a PE is still suspected a two-level PE Wells score should be performed:

Clinical feature	Points
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3
An alternative diagnosis is less likely than PE	3
Heart rate > 100 beats per minute	1.5
Immobilisation for more than 3 days or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Haemoptysis	1
Malignancy (on treatment, treated in the last 6 months, or palliative)	1

Clinical probability simplified scores

- PE likely - more than 4 points
- PE unlikely - 4 points or less

If a PE is 'likely' (more than 4 points) arrange an immediate computed tomography pulmonary angiogram



(CTPA). If there is a delay in getting the CTPA then give low-molecular weight heparin until the scan is performed.

If a PE is 'unlikely' (4 points or less) arranged a D-dimer test. If this is positive arrange an immediate computed tomography pulmonary angiogram (CTPA). If there is a delay in getting the CTPA then give low-molecular weight heparin until the scan is performed.

If the patient has an allergy to contrast media or renal impairment a V/Q scan should be used instead of a CTPA.

### **CTPA or V/Q scan?**

The British Thoracic Society (BTS) published guidelines back in 2003 on the management of patients with suspected pulmonary embolism (PE). Key points from the guidelines include:

- computed tomographic pulmonary angiography (CTPA) is now the recommended initial lung-imaging modality for non-massive PE. Advantages compared to V/Q scans include speed, easier to perform out-of-hours, a reduced need for further imaging and the possibility of providing an alternative diagnosis if PE is excluded
- if the CTPA is negative then patients do not need further investigations or treatment for PE
- ventilation-perfusion scanning may be used initially if appropriate facilities exist, the chest x-ray is normal, and there is no significant symptomatic concurrent cardiopulmonary disease

### **Some other points**

#### **D-dimers**

- sensitivity = 95-98%, but poor specificity

#### **ECG**

- the classic ECG changes seen in PE are a large S wave in lead I, a large Q wave in lead III and an inverted T wave in lead III - 'S1Q3T3'. However this change is seen in no more than 20% of patients
- right bundle branch block and right axis deviation are also associated with PE
- sinus tachycardia may also be seen

#### **V/Q scan**

- sensitivity = 98%; specificity = 40% - high negative predictive value, i.e. if normal virtually excludes PE
- other causes of mismatch in V/Q include old pulmonary embolisms, AV malformations, vasculitis, previous radiotherapy
- COPD gives matched defects

#### **CTPA**

- peripheral emboli affecting subsegmental arteries may be missed

#### **Pulmonary angiography**

- the gold standard
- significant complication rate compared to other investigations

A 70-year-old man who is known to have chronic obstructive pulmonary disease (COPD) is admitted to the Medical Admissions Unit with a suspected infective exacerbation of COPD. What should the target oxygen saturations be until blood gases are available?

<input type="radio"/>	A. >98%
<input type="radio"/>	B. 94-98%
<input type="radio"/>	C. 88-92%
<input type="radio"/>	D. 92-94%
<input type="radio"/>	E. > 95% first 48 hours, > 90% rest of admission

Next question

### Oxygen therapy

The British Thoracic Society published guidelines on emergency oxygen therapy in 2008. The following selected points are taken from the guidelines. Please see the link provided for the full guideline.

**In patients who are critically ill (anaphylaxis, shock etc) oxygen should initially be given via a reservoir mask at 15 l/min. Hypoxia kills.** The BTS guidelines specifically exclude certain conditions where the patient is acutely unwell (e.g. myocardial infarction) but stable.

#### Oxygen saturation targets

- acutely ill patients: 94-98%
- patients at risk of hypercapnia (e.g. COPD patients): 88-92% (see below)
- oxygen should be reduced in stable patients with satisfactory oxygen saturation

#### Management of COPD patients

- prior to availability of blood gases, use a 28% Venturi mask at 4 l/min and aim for an oxygen saturation of 88-92% for patients with risk factors for hypercapnia but no prior history of respiratory acidosis
- adjust target range to 94-98% if the pCO<sub>2</sub> is normal

Situations where oxygen therapy should not be used routinely if there is no evidence of hypoxia:

- myocardial infarction and acute coronary syndromes
- stroke
- obstetric emergencies
- anxiety-related hyperventilation

A 24-year-old male with no past medical history presents to the Emergency Department with pleuritic chest pain. There is no history of a productive cough and he is not short of breath. Chest x-ray shows a right-sided pneumothorax with a 1 cm rim of air and no mediastinal shift. What is the most appropriate management?

<input type="radio"/>	A. Immediate 14G cannula into 2nd intercostal space, mid-clavicular line
<input type="radio"/>	B. Discharge with outpatient chest x-ray
<input type="radio"/>	C. Aspiration
<input type="radio"/>	D. Intercostal drain insertion
<input type="radio"/>	E. Admit for 48 hours observation

[Next question](#)

It would of course be prudent to give advice about what he should do if his symptoms worsen and also suggest routine follow-up with his GP

## Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

### Primary pneumothorax

Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails (defined as > 2 cm or still short of breath) then a chest drain should be inserted

### Secondary pneumothorax

Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and/or the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted if the rim of air is between 1-2cm. If aspiration fails (i.e. pneumothorax is still greater than 1cm) a chest drain should be inserted. All patients should be admitted for at least 24 hours
- if the pneumothorax is less than 1cm then the BTS guidelines suggest giving oxygen and admitting for 24 hours
- regarding scuba diving, the BTS guidelines state: *'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'*

## **Iatrogenic pneumothorax**

Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

**Question 17 of 134**[Next](#)

A 45-year-old man is noted to have bilateral hilar lymphadenopathy on chest x-ray. Which one of the following is the least likely cause?

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. Amyloidosis    |
| <input type="radio"/> | B. Sarcoidosis    |
| <input type="radio"/> | C. Histoplasmosis |
| <input type="radio"/> | D. Tuberculosis   |
| <input type="radio"/> | E. Berylliosis    |

[Next question](#)

Amyloidosis is not commonly associated with bilateral hilar lymphadenopathy

**Bilateral hilar lymphadenopathy**

The most common causes of bilateral hilar lymphadenopathy are sarcoidosis and tuberculosis

Other causes include:

- lymphoma/other malignancy
- pneumoconiosis e.g. berylliosis
- fungi e.g. histoplasmosis, coccidioidomycosis

**Question 18 of 134**

Next

A 41-year-old female presents with 3 day history of a dry cough and shortness of breath. This was preceded by flu-like symptoms. On examination there is a symmetrical, erythematous rash with 'target' lesions over the whole body. What is the likely organism causing the symptoms?

<input type="radio"/>	A. <i>Pseudomonas</i>
<input type="radio"/>	B. <i>Staphylococcus aureus</i>
<input type="radio"/>	C. <i>Mycoplasma pneumoniae</i>
<input type="radio"/>	D. <i>Chlamydia pneumoniae</i>
<input type="radio"/>	E. <i>Legionella pneumophila</i>

Next question

Pneumococcus may also cause erythema multiforme

***Mycoplasma pneumoniae***

*Mycoplasma pneumoniae* is a cause of atypical pneumonia which often affects younger patients. It is associated with a number of characteristic complications such as erythema multiforme and cold autoimmune haemolytic anaemia. Epidemics of *Mycoplasma pneumoniae* classically occur every 4 years. It is important to recognise atypical pneumonias as they may not respond to penicillins or cephalosporins

**Features**

- the disease typically has a prolonged and gradual onset
- flu-like symptoms classically precede a dry cough
- bilateral consolidation on x-ray
- complications may occur as below

**Complications**

- cold agglutins (IgM) may cause an haemolytic anaemia, thrombocytopenia
- erythema multiforme, erythema nodosum
- meningoencephalitis, Guillain-Barre syndrome
- bullous myringitis: painful vesicles on the tympanic membrane
- pericarditis/myocarditis
- gastrointestinal: hepatitis, pancreatitis
- renal: acute glomerulonephritis

**Diagnosis**

- Mycoplasma serology

**Management**

- erythromycin/clarithromycin
- tetracyclines such as doxycycline are an alternative

Which one of the following types of lung cancer is most associated with cavitating lesions?

<input type="radio"/>	A. Carcinoid
<input type="radio"/>	B. Large cell
<input type="radio"/>	C. Small cell
<input type="radio"/>	D. Squamous cell
<input type="radio"/>	E. Adenocarcinoma

Next question

Whilst the other types of lung cancer may cause cavitating lesions, it is most commonly seen in squamous cell cancer

### Chest x-ray: cavitating lung lesion

#### Differential

- abscess (Staph aureus, Klebsiella and *Pseudomonas*)
- squamous cell lung cancer
- tuberculosis
- Wegener's granulomatosis
- pulmonary embolism
- rheumatoid arthritis
- aspergillosis, histoplasmosis, coccidioidomycosis

**Question 20 of 134**

Next

You are reviewing the results from investigations requested at the previous respiratory clinic. A 40-year-old man is being investigated for increasing shortness of breath. The notes show he has smoked for the past 25 years.

Pulmonary function tests reveal the following:

FEV1	1.4 L (predicted 3.8 L)
FVC	1.7 L (predicted 4.5 L)
FEV1/FVC	82% (normal > 75%)

Which one of the following is the most likely explanation?

- ☐ A. Asthma
- ☐ B. Bronchiectasis
- ☐ C. Kyphoscoliosis
- ☐ D. Chronic obstructive pulmonary disease
- ☐ E. Laryngeal malignancy

Next question

These results show a restrictive picture, which may result from a number of conditions including kyphoscoliosis. The other answers cause an obstructive picture.

**Pulmonary function tests**

Pulmonary function tests can be used to determine whether a respiratory disease is obstructive or restrictive. The table below summarises the main findings and gives some example conditions:

Obstructive lung disease	Restrictive lung disease
FEV1 - significantly reduced FVC - reduced or normal FEV1% (FEV1/FVC) - reduced	FEV1 - reduced FVC - significantly reduced FEV1% (FEV1/FVC) - normal or increased
Asthma COPD Bronchiectasis Bronchiolitis obliterans	Pulmonary fibrosis Asbestosis Sarcoidosis Acute respiratory distress syndrome Infant respiratory distress syndrome Kyphoscoliosis Neuromuscular disorders



**Question 21 of 134**

Next

A 46-year-old female with a history of rheumatoid arthritis is investigated due to progressive shortness of breath. She is currently treated with methotrexate and ibuprofen. The following results are obtained from spirometry:

FEV1/FVC	45%
----------	-----

What is the most likely cause of the dyspnoea?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Bronchiolitis obliterans |
| <input type="radio"/> | B. Methotrexate pneumonitis |
| <input type="radio"/> | C. Pulmonary fibrosis       |
| <input type="radio"/> | D. Caplan's syndrome        |
| <input type="radio"/> | E. Lung cancer              |

Next question

The spirometry reveals an obstructive picture which would be in keeping with bronchiolitis obliterans

**Rheumatoid arthritis: respiratory manifestations**

A variety of respiratory problems may be seen in patients with rheumatoid arthritis:

- pulmonary fibrosis
- pleural effusion
- pulmonary nodules
- bronchiolitis obliterans
- complications of drug therapy e.g. methotrexate pneumonitis
- pleurisy
- Caplan's syndrome - massive fibrotic nodules with occupational coal dust exposure
- infection (possibly atypical) secondary to immunosuppression

A 62-year-old female with a 40 pack year history of smoking is investigated for a chronic cough associated with haemoptysis. Bronchoscopy reveals a small 1 cm tumour confined to the right main bronchus. A biopsy taken shows small cell lung cancer. What is the most appropriate management?

<input type="radio"/>	A. Laser therapy
<input type="radio"/>	B. Chemotherapy + radiotherapy
<input type="radio"/>	C. Surgery
<input type="radio"/>	D. Radiotherapy
<input type="radio"/>	E. Interferon-alpha

Next question

Surgery plays little role in the management of small cell lung cancer, with chemotherapy being the mainstay of treatment. Adjuvant radiotherapy is also now given in patients with limited disease.

### Lung cancer: small cell

#### Features

- usually central
- arise from APUD\* cells
- associated with ectopic ADH, ACTH secretion
- ADH --> hyponatraemia
- ACTH --> Cushing's syndrome
- ACTH secretion can cause bilateral adrenal hyperplasia, the high levels of cortisol can lead to hypokalaemic alkalosis
- Lambert-Eaton syndrome: antibodies to voltage gated calcium channels causing myasthenic like syndrome

#### Management

- usually metastatic disease by time of diagnosis
- surgery: only used for debulking
- most patients with limited disease now receive a combination of chemotherapy and radiotherapy
- patients with more extensive disease are offered palliative chemotherapy

\*an acronym for

- Amine - high amine content
- Precursor Uptake - high uptake of amine precursors
- Decarboxylase - high content of the enzyme decarboxylase

**Question 23 of 134**

Next

A 72-year-old man who is known to have chronic kidney disease stage 4 is admitted to the Emergency Department. Since yesterday he has felt short-of-breath on exertion and has been coughing up blood. On examination he tachycardic at 110/min with a normal chest examination. What is the most suitable initial imaging investigation to exclude a pulmonary embolism?

- ☐ A. Ventilation-perfusion scan
- ☐ B. Computed tomographic pulmonary angiography
- ☐ C. Pulmonary angiography
- ☐ D. MRI thorax
- ☐ E. Echocardiogram

Next question

Computed tomographic pulmonary angiography (CTPA) is now used first-line to investigate the possibility of pulmonary embolism. Patients with renal impairment however should be offered Ventilation-perfusion (V/Q) scans as the contrast media used during CTPAs is nephrotoxic.

**Pulmonary embolism: investigation****2012 NICE guidelines**

All patients with symptoms or signs suggestive of a PE should have a history taken, examination performed and a chest x-ray to exclude other pathology.

If a PE is still suspected a two-level PE Wells score should be performed:

Clinical feature	Points
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3
An alternative diagnosis is less likely than PE	3
Heart rate > 100 beats per minute	1.5
Immobilisation for more than 3 days or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Haemoptysis	1
Malignancy (on treatment, treated in the last 6 months, or palliative)	1

**Clinical probability simplified scores**

- PE likely - more than 4 points
- PE unlikely - 4 points or less

If a PE is 'likely' (more than 4 points) arrange an immediate computed tomography pulmonary angiogram (CTPA). If there is a delay in getting the CTPA then give low-molecular weight heparin until the scan is performed.

If a PE is 'unlikely' (4 points or less) arranged a D-dimer test. If this is positive arrange an immediate computed tomography pulmonary angiogram (CTPA). If there is a delay in getting the CTPA then give low-molecular weight heparin until the scan is performed.

If the patient has an allergy to contrast media or renal impairment a V/Q scan should be used instead of a CTPA.

### **CTPA or V/Q scan?**

The British Thoracic Society (BTS) published guidelines back in 2003 on the management of patients with suspected pulmonary embolism (PE). Key points from the guidelines include:

- computed tomographic pulmonary angiography (CTPA) is now the recommended initial lung-imaging modality for non-massive PE. Advantages compared to V/Q scans include speed, easier to perform out-of-hours, a reduced need for further imaging and the possibility of providing an alternative diagnosis if PE is excluded
- if the CTPA is negative then patients do not need further investigations or treatment for PE
- ventilation-perfusion scanning may be used initially if appropriate facilities exist, the chest x-ray is normal, and there is no significant symptomatic concurrent cardiopulmonary disease

### **Some other points**

#### **D-dimers**

- sensitivity = 95-98%, but poor specificity

#### **ECG**

- the classic ECG changes seen in PE are a large S wave in lead I, a large Q wave in lead III and an inverted T wave in lead III - 'S1Q3T3'. However this change is seen in no more than 20% of patients
- right bundle branch block and right axis deviation are also associated with PE
- sinus tachycardia may also be seen

#### **V/Q scan**

- sensitivity = 98%; specificity = 40% - high negative predictive value, i.e. if normal virtually excludes PE
- other causes of mismatch in V/Q include old pulmonary embolisms, AV malformations, vasculitis, previous radiotherapy
- COPD gives matched defects

#### **CTPA**

- peripheral emboli affecting subsegmental arteries may be missed

#### **Pulmonary angiography**

- the gold standard
- significant complication rate compared to other investigations

**Question 24 of 134**

Next

A 62-year-old man who is investigated for haemoptysis is found to have squamous cell lung cancer. Which one of the following is a contraindication to surgery?

<input type="radio"/>	A. Pleural effusion
<input type="radio"/>	B. Superior vena caval obstruction
<input type="radio"/>	C. Haemoptysis
<input type="radio"/>	D. Hypercalcaemia
<input type="radio"/>	E. Enlarged mediastinal lymph nodes

Next question

Contraindications to lung cancer surgery include SVC obstruction, FEV < 1.5, MALIGNANT pleural effusion, and vocal cord paralysis

If one of the options was 'malignant pleural effusion', rather than just 'pleural effusion' (which may be reactive), then this would also be a contraindication

**Lung cancer: non-small cell management****Management**

- only 20% suitable for surgery
- mediastinoscopy performed prior to surgery as CT does not always show mediastinal lymph node involvement
- curative or palliative radiotherapy
- poor response to chemotherapy

**Surgery contraindications**

- assess general health
- stage IIIb or IV (i.e. metastases present)
- FEV1 < 1.5 litres is considered a general cut-off point\*
- malignant pleural effusion
- tumour near hilum
- vocal cord paralysis
- SVC obstruction

\* However if FEV1 < 1.5 for lobectomy or < 2.0 for pneumonectomy then some authorities advocate further lung function tests as operations may still go ahead based on the results

A 24-year-old female with a history of anxiety is taken to the Emergency Department following an acute onset of shortness of breath. On examination the chest is clear to auscultation but the respiratory rate is raised at 40 breaths per minute. A diagnosis of hyperventilation secondary to anxiety is suspected. Which of the following arterial blood gas results (taken on room air) are consistent with this?

<input type="radio"/>	A. pH = 7.56; pCO <sub>2</sub> = 2.9 kPa; pO <sub>2</sub> = 10.1 kPa
<input type="radio"/>	B. pH = 7.24; pCO <sub>2</sub> = 8.4 kPa; pO <sub>2</sub> = 12.7 kPa
<input type="radio"/>	C. pH = 7.34; pCO <sub>2</sub> = 2.7 kPa; pO <sub>2</sub> = 15.4 kPa
<input type="radio"/>	D. pH = 7.54; pCO <sub>2</sub> = 2.4 kPa; pO <sub>2</sub> = 14.1 kPa
<input type="radio"/>	E. pH = 7.54; pCO <sub>2</sub> = 4.9 kPa; pO <sub>2</sub> = 13.3 kPa

[Next question](#)

Hyperventilation will result in carbon dioxide being 'blown off', causing an alkalosis.

Whilst the gases in answer A show a respiratory alkalosis the hypoxia could not be explained by hyperventilation

### Respiratory alkalosis

Common causes

- anxiety leading to hyperventilation
- pulmonary embolism
- salicylate poisoning\*
- CNS disorders: stroke, subarachnoid haemorrhage, encephalitis
- altitude
- pregnancy

\*salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis

**Question 26 of 134**

Next

A 31-year-old woman is referred to the acute medical unit with a 4 day history of polyarthritis and a low-grade pyrexia. Examination reveals shin lesions which the patient states are painful. Chest x-ray shows a bulky mediastinum. What is the most likely diagnosis?

<input type="radio"/>	A. Loffler's syndrome
<input type="radio"/>	B. Lofgren's syndrome
<input type="radio"/>	C. Systemic lupus erythematosus
<input type="radio"/>	D. Gonococcal arthritis
<input type="radio"/>	E. Reiter's syndrome

Next question

Loffler's syndrome is a cause of pulmonary eosinophilia thought to be caused by parasites such as *Ascaris lumbricoides*

**Lofgren's syndrome**

Lofgren's syndrome is an acute form sarcoidosis characterised by bilateral hilar lymphadenopathy (BHL), erythema nodosum, fever and polyarthralgia.

It typically occurs in young females and carries an excellent prognosis

A 24-year-old female comes for review. She was diagnosed with asthma two years ago and is currently using a salbutamol inhaler 100mcg prn combined with beclometasone dipropionate inhaler 200mcg bd. Despite this her asthma is not well controlled. On examination her chest is clear and she has a good inhaler technique. What is the most appropriate next step in management?

- ☐ A. Increase beclometasone dipropionate to 400mcg bd
- ☐ B. Switch steroid to fluticasone propionate
- ☐ C. Trial of leukotriene receptor antagonist
- ☐ D. Add salmeterol
- ☐ E. Add tiotropium

Next question

The British Thoracic Society recommend adding a long-acting B2 agonist if there is an inadequate response to the addition of inhaled steroid. The inhaled steroid dose should be increased if there is an inadequate response to the long-acting B2 agonist.

### Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

<b>Step 1</b>	Inhaled short-acting B2 agonist as required
<b>Step 2</b>	Add inhaled steroid at 200-800 mcg/day*  400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
<b>Step 3</b>	1. Add inhaled long-acting B2 agonist (LABA)  2. Assess control of asthma: <ul style="list-style-type: none"> <li>• good response to LABA - continue LABA</li> <li>• benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose)</li> <li>• no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline</li> </ul>
<b>Step 4</b>	Consider trials of: <ul style="list-style-type: none"> <li>• increasing inhaled steroid up to 2000 mcg/day*</li> <li>• addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet</li> </ul>
<b>Step 5</b>	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets  Maintain high dose inhaled steroid at 2000 mcg/day*  Refer patient for specialist care



\*beclometasone dipropionate or equivalent

## **Additional notes**

Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone

Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles

Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

**Question 28 of 134**

Next

A 31-year-old female with no past medical history of note is admitted to hospital with dyspnoea and fever. She has recently returned from holiday in Turkey. A clinical diagnosis of pneumonia is made. On examination she is noted to have an ulcerated lesion on her upper lip consistent with reactivation of herpes simplex. Which organism is most associated with this examination finding?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. <i>Legionella pneumophila</i>   |
| <input type="radio"/> | B. <i>Staphylococcus aureus</i>    |
| <input type="radio"/> | C. <i>Streptococcus pneumoniae</i> |
| <input type="radio"/> | D. <i>Pneumocystis carinii</i>     |
| <input type="radio"/> | E. <i>Mycoplasma pneumoniae</i>    |

Next question

*Streptococcus pneumoniae* is associated with cold sores

*Streptococcus pneumoniae* commonly causes reactivation of the herpes simplex virus resulting in 'cold sores'

**Pneumonia: community-acquired**

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- *Staphylococcus aureus*: commonly after the 'flu
- atypical pneumonias (e.g. Due to *Mycoplasma pneumoniae*)
- viruses

*Klebsiella pneumoniae* is classically in alcoholics

***Streptococcus pneumoniae* (pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

## Management

The British Thoracic Society published guidelines in 2009:

- low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital
- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin

A 24-year-old woman who is 34 weeks pregnant presents with pleuritic chest pain and shortness of breath. She has noticed some pain in her left calf for the past 3 days and on examination she has clinical signs consistent with a left calf deep vein thrombosis. What is the most appropriate investigation?

- ☐ A. D-dimer
- ☐ B. Compression duplex Doppler
- ☐ C. Computed tomographic pulmonary angiography
- ☐ D. Venogram
- ☐ E. Ventilation-perfusion scan

Next question

Confirming a DVT is the first step as this may provide indirect evidence of a pulmonary embolism. As both conditions require anticoagulation this may negate the need for further radiation exposure.

### Pregnancy: DVT/PE investigation

Guidelines were updated in 2010 by the Royal College of Obstetricians. Key points include:

- chest x-ray should be performed in all patients
- compression duplex Doppler should be performed if the chest x-ray is normal - this may provide indirect evidence of a pulmonary embolism and negate the need for further radiation exposure
- the decision to perform a V/Q or CTPA should be taken at a local level after discussion with the patient and radiologist

### Comparing CTPA to V/Q scanning in pregnancy

CTPA	V/Q scanning
CTPA slightly increases the lifetime risk of <b>maternal breast cancer</b> (increased by up to 13.6%, background risk of 1/200 for study population). Pregnancy makes breast tissue particularly sensitive to the effects of radiation	V/Q scanning carries a slightly increased risk of <b>childhood cancer</b> compared with CTPA (1/280,000 versus less than 1/1,000,000)

D-dimer is of limited use in the investigation of thromboembolism as it is often raised in pregnancy.

Which one of the following paraneoplastic features is least commonly seen in patients with squamous cell lung cancer?

<input type="radio"/>	A. Lambert-Eaton syndrome
<input type="radio"/>	B. Hyperthyroidism
<input type="radio"/>	C. Hypertrophic pulmonary osteoarthropathy
<input type="radio"/>	D. Hypercalcaemia
<input type="radio"/>	E. Clubbing

[Next question](#)

#### Paraneoplastic features of lung cancer

- squamous cell: PTHrp, clubbing, HPOA
- small cell: ADH, ACTH, Lambert-Eaton syndrome

Lambert-Eaton syndrome occurs almost exclusively in small cell lung cancer

#### Lung cancer: paraneoplastic features

##### Small cell

- ADH
- ACTH - not typical, hypertension, hyperglycaemia, hypokalaemia, alkalosis and muscle weakness are more common than buffalo hump etc
- Lambert-Eaton syndrome

##### Squamous cell

- PTH-rp
- clubbing
- hypertrophic pulmonary osteoarthropathy (HPOA)
- hyperthyroidism due to ectopic TSH

##### Adenocarcinoma

- gynaecomastia

An elderly patient with a history of chronic obstructive pulmonary disease is admitted following an infective exacerbation. The posterioranterior (PA) chest x-ray on admission shows a unilateral pleural effusion. Which one of the following is the most useful next line investigation?

<input type="radio"/>	A. Bronchoscopy
<input type="radio"/>	B. Pleural biopsy
<input type="radio"/>	C. Computed tomography
<input type="radio"/>	D. Ultrasound
<input type="radio"/>	E. Lateral chest x-ray

[Next question](#)

Ultrasound is recommended by the British Thoracic Society as it increases the likelihood of successful pleural aspiration and is sensitive for detecting pleural fluid septations.

### Pleural effusion: investigation

The British Thoracic Society (BTS) produced guidelines in 2010 covering the investigation of patients with a pleural effusion.

#### Imaging

- posterioranterior (PA) chest x-rays should be performed in all patients
- ultrasound is recommended: it increases the likelihood of successful pleural aspiration and is sensitive for detecting pleural fluid septations

#### Pleural aspiration

- as above, ultrasound is recommended to reduce the complication rate
- a 21G needle and 50ml syringe should be used
- fluid should be sent for pH, protein, lactate dehydrogenase (LDH), cytology and microbiology

Light's criteria was developed in 1972 to help distinguish between a transudate and an exudate. The BTS recommend using the criteria for borderline cases:

- exudates have a protein level of  $>30$  g/L, transudates have a protein level of  $<30$  g/L
- if the protein level is between 25-35 g/L, Light's criteria should be applied. An exudate is likely if at least one of the following criteria are met:
- pleural fluid protein divided by serum protein  $>0.5$
- pleural fluid LDH divided by serum LDH  $>0.6$
- pleural fluid LDH more than two-thirds the upper limits of normal serum LDH

Other characteristic pleural fluid findings:

- low glucose: rheumatoid arthritis, tuberculosis
- raised amylase: pancreatitis, oesophageal perforation
- heavy blood staining: mesothelioma, pulmonary embolism, tuberculosis

Which one of the following markers is most useful for monitoring the progression of patients with chronic obstructive pulmonary disease?

- ☐ A. FEV1/FVC ratio
- ☐ B. Lifestyle questionnaire
- ☐ C. Oxygen saturations
- ☐ D. FEV1
- ☐ E. Number of exacerbations per year

Next question

### COPD: investigation and diagnosis

NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are smokers or ex-smokers and have symptoms such as exertional breathlessness, chronic cough or regular sputum production.

The following investigations are recommended in patients with suspected COPD:

- post-bronchodilator spirometry to demonstrate airflow obstruction: FEV1/FVC ratio less than 70%
- chest x-ray: hyperinflation, bullae, flat hemidiaphragm. Also important to exclude lung cancer
- full blood count: exclude secondary polycythaemia
- body mass index (BMI) calculation

The severity of COPD is categorised using the FEV1\*:

Post-bronchodilator FEV1/FVC	FEV1 (of predicted)	Severity
< 0.7	> 80%	Stage 1 - Mild**
< 0.7	50-79%	Stage 2 - Moderate
< 0.7	30-49%	Stage 3 - Severe
< 0.7	< 30%	Stage 4 - Very severe

Measuring peak expiratory flow is of limited value in COPD, as it may underestimate the degree of airflow obstruction.

\*note that the grading system has changed following the 2010 NICE guidelines. If the FEV1 is greater than 80% predicted but the post-bronchodilator FEV1/FVC is < 0.7 then this is classified as Stage 1 - mild

\*\*symptoms should be present to diagnose COPD in these patients



**Question 33 of 134**

Next

A 24-year-old male is admitted with acute severe asthma. Treatment is initiated with 100% oxygen, nebulised salbutamol and ipratropium bromide nebulisers and IV hydrocortisone. Despite initial treatment there is no improvement. What is the next step in management?

- ☐ A. IV aminophylline
- ☐ B. IV magnesium sulphate
- ☐ C. IV salbutamol
- ☐ D. Non-invasive ventilation
- ☐ E. IV adrenaline

Next question

Current guidelines do not support the routine use of non-invasive ventilation in asthmatics.

**Asthma: acute severe**

Patients with acute severe asthma are stratified into moderate, severe or life-threatening

Moderate	Severe	Life-threatening
<ul style="list-style-type: none"><li>• PEF &gt; 50% best or predicted</li><li>• Speech normal</li><li>• RR &lt; 25 / min</li><li>• Pulse &lt; 110 bpm</li></ul>	<ul style="list-style-type: none"><li>• PEF 33 - 50% best or predicted</li><li>• Can't complete sentences</li><li>• RR &gt; 25/min</li><li>• Pulse &gt; 110 bpm</li></ul>	<ul style="list-style-type: none"><li>• PEF &lt; 33% best or predicted</li><li>• Oxygen sats &lt; 92%</li><li>• Silent chest, cyanosis or feeble respiratory effort</li><li>• Bradycardia, dysrhythmia or hypotension</li><li>• Exhaustion, confusion or coma</li></ul>

**British Thoracic Society guidelines**

- magnesium sulphate recommended as next step for patients who are not responding (e.g. 1.2 - 2g IV over 20 mins)
- little evidence to support use of IV aminophylline (although still mentioned in management plans)
- if no response consider IV salbutamol

A 29-year-old man presents to the Emergency Department with dyspnoea. He has no past medical history of note other than a fractured ankle five months ago. On examination he has reduced breath sounds on the left side. The trachea is central and oxygen saturations are 98% on room air. A chest x-ray shows a pneumothorax on the left-side with a 3.5cm rim of air. There is no midline shift. What is the most appropriate initial management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Aspiration  |
| <input type="radio"/> | B. Chest drain   |
| <input type="radio"/> | C. Discharge with outpatient follow-up x-ray                           |
| <input type="radio"/> | D. Give 28% oxygen via a Venturi mask                                  |
| <input type="radio"/> | E. Insert a cannula into the 2nd intercostal space, midclavicular line |

[Next question](#)

The British Thoracic Society (BTS) guidelines would advocate aspiration in this scenario given the absence of a secondary cause, for example asthma. In accordance with the BTS oxygen guidelines there are no indications to give oxygen.

### Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

#### Primary pneumothorax

Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails (defined as > 2 cm or still short of breath) then a chest drain should be inserted

#### Secondary pneumothorax

Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and/or the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted if the rim of air is between 1-2cm. If aspiration fails (i.e. pneumothorax is still greater than 1cm) a chest drain should be inserted. All patients should be admitted for at least 24 hours
- if the pneumothorax is less than 1cm then the BTS guidelines suggest giving oxygen and admitting for 24 hours

- regarding scuba diving, the BTS guidelines state: *'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'*

## **Iatrogenic pneumothorax**

Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

**Question 35 of 134**

Next

A 24-year-old heroin addict is admitted following an overdose. He is drowsy and has a respiratory rate of 6 / min. Which of the following arterial blood gas results (taken on room air) are most consistent with this?

<input type="radio"/>	A. pH = 7.49; pCO <sub>2</sub> = 4.9 kPa; pO <sub>2</sub> = 10.1 kPa
<input type="radio"/>	B. pH = 7.52; pCO <sub>2</sub> = 2.9 kPa; pO <sub>2</sub> = 13.1 kPa
<input type="radio"/>	C. pH = 7.31; pCO <sub>2</sub> = 7.4 kPa; pO <sub>2</sub> = 8.1 kPa
<input type="radio"/>	D. pH = 7.55; pCO <sub>2</sub> = 3.4 kPa; pO <sub>2</sub> = 14.3 kPa
<input type="radio"/>	E. pH = 7.32; pCO <sub>2</sub> = 3.4 kPa; pO <sub>2</sub> = 8.3 kPa

Next question

This patient is likely to have developed a respiratory acidosis secondary to hypoventilation.

**Respiratory acidosis**

Respiratory acidosis may be caused by a number of conditions

- COPD
- decompensation in other respiratory conditions e.g. Life-threatening asthma / pulmonary oedema
- sedative drugs: benzodiazepines, opiate overdose

**Question 36 of 134**

Next

A 20-year-old man who has a family history of alpha-1 antitrypsin deficiency has genetic testing. The following results are received:

A1AT genotype	PiMZ
---------------	------

What is the most likely outcome?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Weekly intravenous alpha1-antitrypsin protein concentrates in later life |
| <input type="radio"/> | B. Mild emphysema controlled with bronchodilator therapy                    |
| <input type="radio"/> | C. Death within 5-10 years  |
| <input type="radio"/> | D. Lung transplantation in later life                                       |
| <input type="radio"/> | E. No evidence of lung disease  |

Next question

Heterozygote patients such as those with the PiMZ genotype have alpha-1 antitrypsin levels approximately 35% of normal. They therefore have a low risk of developing clinically evident lung disease.

**Alpha-1 antitrypsin deficiency**

Alpha-1 antitrypsin (A1AT) deficiency is a common inherited condition caused by a lack of a protease inhibitor (Pi) normally produced by the liver. The role of A1AT is to protect cells from enzymes such as neutrophil elastase.

**Genetics**

- located on chromosome 14
- inherited in an autosomal recessive / co-dominant fashion\*
- alleles classified by their electrophoretic mobility - M for normal, S for slow, and Z for very slow
- normal = PiMM
- homozygous PiSS (50% normal A1AT levels)
- homozygous PiZZ (10% normal A1AT levels)

**Features**

- patients who manifest disease usually have PiZZ genotype
- lungs: panacinar emphysema, most marked in lower lobes
- liver: cirrhosis and hepatocellular carcinoma in adults, cholestasis in children

**Investigations**

- A1AT concentrations

## Management

- no smoking
- supportive: bronchodilators, physiotherapy
- intravenous alpha1-antitrypsin protein concentrates
- surgery: volume reduction surgery, lung transplantation

\*trusted sources are split on which is a more accurate description

A 19-year-old man presents as he is concerned he may be asthmatic. Which one of the following points in the history would make this diagnosis less likely?

- ☐ A. Smoking since age of 16 years
- ☐ B. Peripheral tingling during episodes of dyspnoea
- ☐ C. Peripheral blood eosinophilia
- ☐ D. Chest tightness whilst exercising
- ☐ E. History of eczema

Next question

The British Thoracic Society suggest peripheral tingling is one of the factors which makes a diagnosis of asthma less likely. His smoking history does not preclude a diagnosis of asthma

### Asthma: diagnosis in adults

The 2008 British Thoracic Society guidelines marked a subtle change in the approach to diagnosing asthma. This approach is supported in the updated 2011 guidelines. It suggests dividing patients into a high, intermediate and low probability of having asthma based on the presence or absence of typical symptoms. A list can be found in the external link but include typical symptoms such as wheeze, nocturnal cough etc

Example of features used to assess asthma (not complete, please see link)

Increase possibility of asthma	Decrease possibility of asthma
<ul style="list-style-type: none"> <li>• Wheeze, breathlessness, chest tightness and cough, worse at night/early morning</li> <li>• History of atopic disorder</li> <li>• Wheeze heard on auscultation</li> <li>• Unexplained peripheral blood eosinophilia</li> </ul>	<ul style="list-style-type: none"> <li>• Prominent dizziness, light-headedness, peripheral tingling</li> <li>• Chronic productive cough in the absence of wheeze or breathlessness</li> <li>• Repeatedly normal physical examination</li> <li>• Significant smoking history (i.e. &gt; 20 pack-years)</li> <li>• Normal PEF or spirometry when symptomatic</li> </ul>

Management is based on this assessment:

- high probability: trial of treatment
- intermediate probability: see below
- low probability: investigate/treat other condition

For patients with an intermediate probability of asthma further investigations are suggested. The guidelines state that spirometry is the preferred initial test:

- FEV1/FVC < 0.7: trial of treatment
- FEV1/FVC > 0.7: further investigation/consider referral

Recent studies have shown the limited value of other 'objective' tests. It is now recognised that in patients with normal or near-normal pre-treatment lung function there is little room for measurable improvement in FEV1 or peak flow.

A > 400 ml improvement in FEV1 is considered significant

- before and after 400 mcg inhaled salbutamol in patients with diagnostic uncertainty and airflow obstruction present at the time of assessment
- if there is an incomplete response to inhaled salbutamol, after either inhaled corticosteroids (200 mcg twice daily beclometasone equivalent for 6-8 weeks) or oral prednisolone (30 mg once daily for 14 days)

It is now advised to interpret peak flow variability with caution due to the poor sensitivity of the test

- diurnal variation % =  $[(\text{Highest} - \text{Lowest PEFr}) / \text{Highest PEFr}] \times 100$
- assessment should be made over 2 weeks
- greater than 20% diurnal variation is considered significant



Which one of the following is least associated with Kartagener's syndrome?

<input type="radio"/>	A. Male subfertility
<input type="radio"/>	B. Recurrent sinusitis
<input type="radio"/>	C. Malabsorption
<input type="radio"/>	D. Dextrocardia
<input type="radio"/>	E. Bronchiectasis

Next question

### Kartagener's syndrome

Kartagener's syndrome (also known as primary ciliary dyskinesia) was first described in 1933 and most frequently occurs in examinations due to its association with dextrocardia (e.g. 'quiet heart sounds', 'small volume complexes in lateral leads')

#### Features

- dextrocardia or complete situs inversus
- bronchiectasis
- recurrent sinusitis
- subfertility (secondary to diminished sperm motility and defective ciliary action in the fallopian tubes)

A 44-year-old man who is known to be HIV positive presents with shortness-of-breath. Which one of the following features is most characteristic of *Pneumocystis carinii* pneumonia?

<input type="radio"/>	A. Usually occurs when the CD4 count is 200-300/mm <sup>3</sup>
<input type="radio"/>	B. Absence of fever
<input type="radio"/>	C. Productive cough
<input type="radio"/>	D. Oxygen saturations usually improve after short period of exertion
<input type="radio"/>	E. Normal chest auscultation

[Next question](#)

### HIV: *Pneumocystis jiroveci* pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as *Pneumocystis jiroveci*, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- *Pneumocystis jiroveci* is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count < 200/mm<sup>3</sup> should receive PCP prophylaxis

#### Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Extrapulmonary manifestations are rare (1-2% of cases), may cause

- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

#### Investigation

- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal
- exercise-induced desaturation

- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain)

## Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if  $pO_2 < 9.3\text{kPa}$  then steroids reduce risk of respiratory failure by 50% and death by a third)

A 52-year-old woman with a history of breast cancer is admitted with acute dyspnoea. Her respiratory rate on admission is 42 / min and her oxygen saturations are 87% on room air. A pulmonary embolism is suspected and she is transferred to the high dependency unit after being treated with oxygen and enoxaparin. Which one of the following would be strongest indication for thrombolysis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Extensive deep venous thrombosis          |
| <input type="radio"/> | B. Hypotension                               |
| <input type="radio"/> | C. Patient choice following informed consent |
| <input type="radio"/> | D. Hypoxaemia despite high flow oxygen       |
| <input type="radio"/> | E. ECG showing right ventricular strain      |

[Next question](#)

Massive PE + hypotension - thrombolyse

### Pulmonary embolism: management

The NICE guidelines of 2012 provided some clarity on how long patients should be anticoagulated for after a pulmonary embolism (PE). Selected points are listed below.

Low molecular weight heparin (LMWH) or fondaparinux should be given initially after a PE is diagnosed. An exception to this is for patients with a massive PE where thrombolysis is being considered. In such a situation unfractionated heparin should be used.

- a vitamin K antagonist (i.e. warfarin) should be given within 24 hours of the diagnosis
- the LMWH or fondaparinux should be continued for at least 5 days or until the international normalised ratio (INR) is 2.0 or above for at least 24 hours, whichever is longer, i.e. LMWH or fondaparinux is given at the same time as warfarin until the INR is in the therapeutic range
- warfarin should be continued for at least 3 months. At 3 months, NICE advise that clinicians should 'assess the risks and benefits of extending treatment'
- NICE advise extending warfarin beyond 3 months for patients with *unprovoked* PE. This essentially means that if there was no obvious cause or provoking factor (surgery, trauma, significant immobility) it may imply the patient has a tendency to thrombosis and should be given treatment longer than the norm of 3 months
- for patients with active cancer NICE recommend using LMWH for 6 months

### Thrombolysis

- thrombolysis is now recommended as the first-line treatment for massive PE where there is circulatory failure (e.g. hypotension). Other invasive approaches should be considered where appropriate facilities exist

A 67-year-old female is referred to the acute medical unit with an infective exacerbation of COPD. Despite maximal medical therapy the arterial blood gases continue to show type II respiratory failure. You are asked to consider non-invasive ventilation. At what pH is the patient most likely to receive benefit from non-invasive ventilation?

- |                       |            |
|-----------------------|------------|
| <input type="radio"/> | A. pH 7.13 |
| <input type="radio"/> | B. pH 7.18 |
| <input type="radio"/> | C. pH 7.23 |
| <input type="radio"/> | D. pH 7.29 |
| <input type="radio"/> | E. pH 7.37 |

[Next question](#)

The evidence surrounding the use of NIV in COPD shows that patients with a pH in the range of 7.25-7.35 achieve the most benefit. If the pH is < 7.25 then invasive ventilation should be considered if appropriate

### Non-invasive ventilation

The British Thoracic Society (BTS) published guidelines in 2002 on the use of non-invasive ventilation in acute respiratory failure. Following these the Royal College of Physicians published guidelines in 2008.

Non-invasive ventilation - key indications

- COPD with respiratory acidosis pH 7.25-7.35
- type II respiratory failure secondary to chest wall deformity, neuromuscular disease or obstructive sleep apnoea
- cardiogenic pulmonary oedema unresponsive to CPAP
- weaning from tracheal intubation

Recommended initial settings for bi-level pressure support in COPD

- Expiratory Positive Airway Pressure (EPAP): 4-5 cm H<sub>2</sub>O
- Inspiratory Positive Airway Pressure (IPAP): RCP advocate 10 cm H<sub>2</sub>O whilst BTS suggest 12-15 cm H<sub>2</sub>O
- back up rate: 15 breaths/min
- back up inspiration:expiration ratio: 1:3

A 35-year-old female with sarcoidosis is started on a course of prednisolone. Which one of the following is a suitable indication for commencing steroid therapy in such patients?

<input type="radio"/>	A. Bilateral hilar lymphadenopathy
<input type="radio"/>	B. Arthralgia
<input type="radio"/>	C. Hypercalcaemia
<input type="radio"/>	D. Serum ACE > 120 u/l
<input type="radio"/>	E. Erythema nodosum

[Next question](#)

### Sarcoidosis: management

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas. It is more common in young adults and in people of African descent

Indications for steroids

- hypercalcaemia
- worsening lung function
- eye, heart or neuro involvement

**Question 43 of 134**

Next

A 54-year-old man is investigated for a chronic cough. A chest x-ray arranged by his GP shows a suspicious lesion in the right lung. He has no past history of note and is a life-long non-smoker. An urgent bronchoscopy is arranged which is normal. What is the most likely diagnosis?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Lung sarcoma              |
| <input type="radio"/> | B. Squamous cell lung cancer |
| <input type="radio"/> | C. Lung adenocarcinoma       |
| <input type="radio"/> | D. Small cell lung cancer    |
| <input type="radio"/> | E. Lung carcinoid            |

Next question

**Lung adenocarcinoma**

- most common type in non-smokers
- peripheral lesion

The clues are the absence of a smoking history and normal bronchoscopy, which suggests a peripherally located lesion.

**Lung cancer: non-small cell**

There are three main subtypes of non-small cell lung cancer:

**Squamous cell cancer**

- typically central
- associated with ectopic PTH secretion --> hypercalcaemia
- strongly associated with finger clubbing
- hypertrophic pulmonary osteoarthropathy (HPOA)

**Adenocarcinoma**

- most common type of lung cancer in non-smokers, although the majority of patients who develop lung adenocarcinoma are smokers
- typically located on the lung periphery

**Large cell lung carcinoma**

A 45-year-old dairy farmer presents with increasing shortness-of-breath on exertion. He is a non-smoker and has no respiratory history of note. His symptoms seem to become much worse when he is around the farm and are associated with chest tightness and a non-productive cough. A diagnosis of extrinsic allergic alveolitis is suspected. Which one of the following is most likely to be responsible?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. <i>Mycoplasma pneumoniae</i>   |
| <input type="radio"/> | B. Isocyanate based pesticides    |
| <input type="radio"/> | C. Contaminated hay               |
| <input type="radio"/> | D. Cow faeces                     |
| <input type="radio"/> | E. Ryegrass ( <i>Lolium sp.</i> ) |

Next question

Contaminated hay is the most common source of *Saccharopolyspora rectivirgula* which is responsible for Farmer's lung.

### Extrinsic allergic alveolitis

Extrinsic allergic alveolitis (EAA, also known as hypersensitivity pneumonitis) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles. It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase.

#### Examples

- bird fanciers' lung: avian proteins
- farmers lung: spores of *Saccharopolyspora rectivirgula* (formerly *Micropolyspora faeni*)
- malt workers' lung: *Aspergillus clavatus*
- mushroom workers' lung: thermophilic actinomycetes\*

#### Presentation

- acute: occur 4-8 hrs after exposure, SOB, dry cough, fever
- chronic

#### Investigation

- chest x-ray: upper lobe fibrosis
- bronchoalveolar lavage: lymphocytosis
- blood: NO eosinophilia

\*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as *Micropolyspora faeni*



A 62-year-old female is admitted with a suspected infective exacerbation of COPD. A chest x-ray shows no evidence of consolidation. What is the most likely causative organism?

<input type="radio"/>	A. <i>Pseudomonas aeruginosa</i>
<input type="radio"/>	B. <i>Haemophilus influenzae</i>
<input type="radio"/>	C. <i>Staphylococcus aureus</i>
<input type="radio"/>	D. <i>Streptococcus pneumoniae</i>
<input type="radio"/>	E. <i>Moraxella catarrhalis</i>

[Next question](#)

If the patient had pneumonia then *Streptococcus pneumoniae* would be the most likely causative organism. However, the chest x-ray shows no evidence of consolidation making a diagnosis of pneumonia unlikely.

*Haemophilus influenzae* is the most common cause of infective exacerbations of COPD. The patient should be treated with a course of amoxicillin or a tetracycline together with prednisolone.

#### COPD: management of acute exacerbations

The most common bacterial organisms that cause infective exacerbations of COPD are:

- *Haemophilus influenzae* (most common cause)
- *Streptococcus pneumoniae*
- *Moraxella catarrhalis*

Respiratory viruses account for around 30% of exacerbations, with the human rhinovirus being the most important pathogen.

NICE guidelines from 2010 recommend the following:

- increase frequency of bronchodilator use and consider giving via a nebuliser
- give prednisolone 30 mg daily for 7-14 days
- it is common practice for all patients with an exacerbation of COPD to receive antibiotics. NICE do not support this approach. They recommend giving oral antibiotics 'if sputum is purulent or there are clinical signs of pneumonia'

**Question 46 of 134**

Next

You review a 67-year-old man who has chronic obstructive pulmonary disease (COPD). On examination there is evidence of cor pulmonale with a significant degree of pedal oedema. His FEV1 is 43%. During a recent hospital stay his pO<sub>2</sub> on room air was 7.5 kPa. Which one of the following interventions is most likely to increase survival in this patient?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Inhaled corticosteroid   |
| <input type="radio"/> | B. Heart-lung transplant    |
| <input type="radio"/> | C. Pulmonary rehabilitation |
| <input type="radio"/> | D. Loop diuretic therapy    |
| <input type="radio"/> | E. Long-term oxygen therapy |

Next question

After smoking cessation, long-term oxygen therapy (LTOT) is one of the few interventions that has been shown to improve survival in COPD.

LTOT should be offered to patients with a pO<sub>2</sub> of < 7.3 kPa or to those with a pO<sub>2</sub> of 7.3 - 8 kPa and one of the following:

- secondary polycythaemia
- nocturnal hypoxaemia
- peripheral oedema
- pulmonary hypertension

**COPD: stable management**

NICE updated its guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

**General management**

- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

**Bronchodilator therapy**

- a short-acting beta<sub>2</sub>-agonist (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV<sub>1</sub>

FEV1 > 50%

- long-acting beta2-agonist (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%

- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness

- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline

- NICE only recommends theophylline after trials of short and long-acting bronchodilators or to people who cannot use inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics

- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale

- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD

- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

A 49-year-old male with a past history of alcohol excess presents to the Emergency Department due to fever and shortness of breath. Chest x-ray reveals a cavitating lesion in the right middle zone. What is the most likely causative organism?

<input type="radio"/>	A. <i>Klebsiella</i>
<input type="radio"/>	B. <i>Bartonella</i>
<input type="radio"/>	C. <i>Pneumococcus</i>
<input type="radio"/>	D. <i>Coxiella burnetii</i>
<input type="radio"/>	E. <i>Haemophilus influenzae</i>

[Next question](#)

*Klebsiella pneumoniae* (Friedlander's pneumonia) typically occurs in middle-aged alcoholic men. Chest x-ray features may include abscess formation in the middle/upper lobes and empyema. The mortality approaches 30-50%

#### Chest x-ray: cavitating lung lesion

##### Differential

- abscess (*Staph aureus*, *Klebsiella* and *Pseudomonas*)
- squamous cell lung cancer
- tuberculosis
- Wegener's granulomatosis
- pulmonary embolism
- rheumatoid arthritis
- aspergillosis, histoplasmosis, coccidioidomycosis

**Question 48 of 134**

Next

A 55-year-old man is referred to the medical admissions unit. He recently returned from a holiday in Italy and has failed to respond to a course of co-amoxiclav for a suspected lower respiratory tract infection. Chest x-ray shows bilateral infiltrates. Bloods are as follows:

Na <sup>+</sup>	122 mmol/l
K <sup>+</sup>	4.3 mmol/l
Urea	8.4 mmol/l
Creatinine	130 µmol/l

What is the likely diagnosis?

- ☐ A. Goodpasture's syndrome
- ☐ B. Legionella pneumonia
- ☐ C. *Pneumocystis carinii* pneumonia
- ☐ D. Pulmonary eosinophilia
- ☐ E. Mycoplasma pneumonia

Next question

**Legionella**

Legionnaire's disease is caused by the intracellular bacterium *Legionella pneumophila*. It typically colonizes water tanks and hence questions may hint at air-conditioning systems or foreign holidays. Person-to-person transmission is not seen

**Features**

- flu-like symptoms
- dry cough
- relative bradycardia
- confusion
- lymphopenia
- hyponatraemia
- deranged LFTs

**Diagnosis**

- urinary antigen

**Management**

- treat with erythromycin

Each one of the following may result in bronchiectasis, except:

<input type="radio"/>	A. Kartagener's syndrome
<input type="radio"/>	B. Amyloidosis
<input type="radio"/>	C. Selective IgA deficiency
<input type="radio"/>	D. Lung cancer
<input type="radio"/>	E. Allergic bronchopulmonary aspergillosis

Next question

Amyloidosis does not cause bronchiectasis per se, but may be seen in bronchiectasis as a consequence of chronic inflammation and infection

### Bronchiectasis: causes

Bronchiectasis describes a permanent dilatation of the airways secondary to chronic infection or inflammation. There are a wide variety of causes are listed below:

#### Causes

- post-infective: tuberculosis, measles, pertussis, pneumonia
- cystic fibrosis
- bronchial obstruction e.g. lung cancer/foreign body
- immune deficiency: selective IgA, hypogammaglobulinaemia
- allergic bronchopulmonary aspergillosis (ABPA)
- ciliary dyskinetic syndromes: Kartagener's syndrome, Young's syndrome
- yellow nail syndrome

Which one of the following causes of lung fibrosis predominately affect the lower zones?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Methotrexate                  |
| <input type="radio"/> | B. Sarcoidosis                   |
| <input type="radio"/> | C. Coal worker's pneumoconiosis  |
| <input type="radio"/> | D. Ankylosing spondylitis        |
| <input type="radio"/> | E. Extrinsic allergic alveolitis |

Next question

### Lung fibrosis

It is important in the exam to be able to differentiate between conditions causing predominately upper or lower zone fibrosis. It should be noted that the more common causes (cryptogenic fibrosing alveolitis, drugs) tend to affect the lower zones

Fibrosis predominately affecting the upper zones

- extrinsic allergic alveolitis
- coal worker's pneumoconiosis/progressive massive fibrosis
- silicosis
- sarcoidosis
- ankylosing spondylitis (rare)
- histiocytosis
- tuberculosis

Fibrosis predominately affecting the lower zones

- cryptogenic fibrosing alveolitis
- most connective tissue disorders (except ankylosing spondylitis)
- drug-induced: amiodarone, bleomycin, methotrexate
- asbestosis

A preliminary diagnosis of extrinsic allergic alveolitis in a 55-year-old man. Which one of the following features would most support this diagnosis?

<input type="radio"/>	A. Clubbing
<input type="radio"/>	B. Eosinophilia
<input type="radio"/>	C. Cyanosis
<input type="radio"/>	D. Fibrosis in the upper zones
<input type="radio"/>	E. History of working in the steel industry

Next question

A history of working in the steel industry and eosinophilia are not features of extrinsic allergic alveolitis. Clubbing and cyanosis are non-specific

### Extrinsic allergic alveolitis

Extrinsic allergic alveolitis (EAA, also known as hypersensitivity pneumonitis) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles. It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase.

#### Examples

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- acute: occur 4-8 hrs after exposure, SOB, dry cough, fever
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#### Investigation

- chest x-ray: upper lobe fibrosis
- bronchoalveolar lavage: lymphocytosis
- blood: NO eosinophilia

\*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as *Micropolyspora faeni*



You are reviewing the management of a number of patients with chronic obstructive pulmonary disease (COPD). Which one of the following factors should prompt an assessment for long-term oxygen therapy?

<input type="radio"/>	A. FEV1 54% of predicted
<input type="radio"/>	B. Haemoglobin of 18.4 g/dl
<input type="radio"/>	C. Body mass index 18.8 kg / m <sup>2</sup>
<input type="radio"/>	D. Oxygen saturations of 93% on room air
<input type="radio"/>	E. FEV1/FVC of 0.47

[Next question](#)

### COPD: long-term oxygen therapy

The 2010 NICE guidelines on COPD clearly define which patients should be assessed for and offered long-term oxygen therapy (LTOT). Patients who receive LTOT should breathe supplementary oxygen for at least 15 hours a day. Oxygen concentrators are used to provide a fixed supply for LTOT.

Assess patients if any of the following:

- very severe airflow obstruction (FEV1 < 30% predicted). Assessment should be 'considered' for patients with severe airflow obstruction (FEV1 30-49% predicted)
- cyanosis
- polycythaemia
- peripheral oedema
- raised jugular venous pressure
- oxygen saturations less than or equal to 92% on room air

Assessment is done by measuring arterial blood gases on 2 occasions at least 3 weeks apart in patients with stable COPD on optimal management.

Offer LTOT to patients with a pO<sub>2</sub> of < 7.3 kPa or to those with a pO<sub>2</sub> of 7.3 - 8 kPa and one of the following:

- secondary polycythaemia
- nocturnal hypoxaemia
- peripheral oedema
- pulmonary hypertension

Each one of the following predisposes to the development of obstructive sleep apnoea, except:

<input type="radio"/>	A. Acromegaly
<input type="radio"/>	B. Chronic obstructive pulmonary disease
<input type="radio"/>	C. Amyloidosis
<input type="radio"/>	D. Obesity
<input type="radio"/>	E. Hypothyroidism

Next question

Sleep apnoea causes include obesity and macroglossia

The Sleep Heart Health Study showed that when these two conditions do coexist, this is the result of chance alone

### Obstructive sleep apnoea/hypopnoea syndrome

Predisposing factors

- obesity
- macroglossia: acromegaly, hypothyroidism, amyloidosis
- large tonsils
- Marfan's syndrome

Consequence

- daytime somnolence
- hypertension

SIGN guidelines for the diagnosis and management of patients with OSAHS were published in 2003

Assessment of sleepiness

- Epworth Sleepiness Scale - questionnaire completed by patient +/- partner
- Multiple Sleep Latency Test (MSLT) - measures the time to fall asleep in a dark room (using EEG criteria)

Diagnostic tests

- sleep studies - ranging from monitoring of pulse oximetry at night to full polysomnography where a wide variety of physiological factors are measured including EEG, respiratory airflow, thoraco-abdominal movement, snoring and pulse oximetry

## Management

- weight loss
- CPAP is first line for moderate or severe OSAHS
- intra-oral devices (e.g. mandibular advancement) may be used if CPAP is not tolerated or for patients with mild OSAHS where there is no daytime sleepiness
- limited evidence to support use of pharmacological agents

Which one of the following is not part of the diagnostic criteria of acute respiratory distress syndrome (ARDS)?

<input type="radio"/>	A. Bilateral infiltrates on CXR
<input type="radio"/>	B. Non-cardiogenic
<input type="radio"/>	C. $pO_2/FiO_2 < 200$ mmHg
<input type="radio"/>	D. Respiratory rate $> 24/\text{min}$
<input type="radio"/>	E. Acute onset

Next question

## ARDS

### Basics

- acute respiratory distress syndrome
- caused by increased permeability of alveolar capillaries leading to fluid accumulation in alveoli i.e. non-cardiogenic pulmonary oedema

### Criteria (American-European Consensus Conference)

- acute onset
- bilateral infiltrates on CXR
- non-cardiogenic (pulmonary artery wedge pressure needed if doubt)
- $pO_2/FiO_2 < 200$  mmHg

### Causes

- infection: sepsis, pneumonia
- massive blood transfusion
- trauma
- smoke inhalation
- pancreatitis
- cardio-pulmonary bypass

**Question 55 of 134**

Next

A 62-year-old man with a history of recurrent lower respiratory tract infections is diagnosed as having bilateral bronchiectasis following a high resolution CT scan. Which one of the following is most important in the long term control of his symptoms?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Inhaled corticosteroids  |
| <input type="radio"/> | B. Prophylactic antibiotics |
| <input type="radio"/> | C. Surgery                  |
| <input type="radio"/> | D. Postural drainage        |
| <input type="radio"/> | E. Mucolytic therapy        |

Next question

Symptom control in non-CF bronchiectasis - inspiratory muscle training + postural drainage

**Bronchiectasis: management**

Bronchiectasis describes a permanent dilatation of the airways secondary to chronic infection or inflammation. After assessing for treatable causes (e.g. immune deficiency) management is as follows:

- physical training (e.g. inspiratory muscle training) - has a good evidence base for patients with non-cystic fibrosis bronchiectasis
- postural drainage
- antibiotics for exacerbations + long-term rotating antibiotics in severe cases
- bronchodilators in selected cases
- immunisations
- surgery in selected cases (e.g. Localised disease)

Most common organisms isolated from patients with bronchiectasis:

- *Haemophilus influenzae* (most common)
- *Pseudomonas aeruginosa*
- *Klebsiella* spp.
- *Streptococcus pneumoniae*

Which one the following statements regarding asbestos is not correct?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Pleural plaques are premalignant                            |
| <input type="radio"/> | B. Asbestosis typically affects the lower zones                |
| <input type="radio"/> | C. Crocidolite (blue) asbestos is the most dangerous form      |
| <input type="radio"/> | D. Severity of asbestosis is related to the length of exposure |
| <input type="radio"/> | E. Mesothelioma may develop following minimal exposure         |

[Next question](#)

## Asbestos and the lung

Asbestos can cause a variety of lung disease from benign pleural plaques to mesothelioma.

### Pleural plaques

Pleural plaques are benign and do not undergo malignant change. They are the most common form of asbestos related lung disease and generally occur after a latent period of 20-40 years.

### Pleural thickening

Asbestos exposure may cause diffuse pleural thickening in a similar pattern to that seen following an empyema or haemothorax. The underlying pathophysiology is not fully understood.

### Asbestosis

The severity of asbestosis is related to the length of exposure. This is in contrast to mesothelioma where even very limited exposure can cause disease. The latent period is typically 15-30 years. Asbestosis typically causes lower lobe fibrosis. As with other forms of lung fibrosis the most common symptoms are shortness-of-breath and reduced exercise tolerance.

### Mesothelioma

Mesothelioma is a malignant disease of the pleura. Crocidolite (blue) asbestos is the most dangerous form.

Possible features

- progressive shortness-of-breath
- chest pain
- pleural effusion

Patients are usually offered palliative chemotherapy and there is also a limited role for surgery and radiotherapy. Unfortunately the prognosis is very poor, with a median survival from diagnosis of 8-14 months.

### Lung cancer

Asbestos exposure is a risk factor for lung cancer and also has a synergistic effect with cigarette smoke.

Which of the following features is associated with a good prognosis in sarcoidosis?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Insidious onset           |
| <input type="radio"/> | B. Splenomegaly              |
| <input type="radio"/> | C. Disease in black people   |
| <input type="radio"/> | D. Stage III features on CXR |
| <input type="radio"/> | E. Erythema nodosum          |

Next question

Erythema nodosum is associated with a good prognosis in sarcoidosis

### Sarcoidosis: prognostic features

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas. It is more common in young adults and in people of African descent. Sarcoidosis remits without treatment in approximately two-thirds of people

Factors associated with poor prognosis

- insidious onset, symptoms > 6 months
- absence of erythema nodosum
- extrapulmonary manifestations: e.g. lupus pernio, splenomegaly
- CXR: stage III-IV features
- black people

A 43-year-old man is admitted due to shortness of breath and is noted to have a cavitating lesion on his chest x-ray. Which one of the following conditions is not part of the differential diagnosis?

<input type="radio"/>	A. Lung cancer
<input type="radio"/>	B. Pulmonary embolism
<input type="radio"/>	C. Wegener's granulomatosis
<input type="radio"/>	D. Churg-Strauss syndrome
<input type="radio"/>	E. Tuberculosis

[Next question](#)

### Chest x-ray: cavitating lung lesion

#### Differential

- abscess (*Staph aureus*, *Klebsiella* and *Pseudomonas*)
- squamous cell lung cancer
- tuberculosis
- Wegener's granulomatosis
- pulmonary embolism
- rheumatoid arthritis
- aspergillosis, histoplasmosis, coccidioidomycosis



A 45-year-old woman who is a known asthmatic comes for review. In the past two years she has had around six exacerbations of asthma requiring oral steroids. Her current medication includes salbutamol 2 puffs prn, salmeterol 50mcg bd and beclometasone 200 mcg 1 puff bd. You note from the records that her BMI is 31 kg/m<sup>2</sup>, she is a non-smoker and has a good inhaler technique. What is the most appropriate next step in management?

- ☐ A. Increase beclometasone to 200 mcg 2 puffs bd
- ☐ B. Referral to a dietician
- ☐ C. Add oral theophylline
- ☐ D. Add oral montelukast
- ☐ E. Add inhaled tiotropium

[Next question](#)

### Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

<b>Step 1</b>	Inhaled short-acting B2 agonist as required
<b>Step 2</b>	Add inhaled steroid at 200-800 mcg/day*  400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
<b>Step 3</b>	1. Add inhaled long-acting B2 agonist (LABA)  2. Assess control of asthma: <ul style="list-style-type: none"> <li>• good response to LABA - continue LABA</li> <li>• benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose)</li> <li>• no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline</li> </ul>
<b>Step 4</b>	Consider trials of: <ul style="list-style-type: none"> <li>• increasing inhaled steroid up to 2000 mcg/day*</li> <li>• addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet</li> </ul>
<b>Step 5</b>	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets  Maintain high dose inhaled steroid at 2000 mcg/day*  Refer patient for specialist care

\*beclometasone dipropionate or equivalent

## **Additional notes**

Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone

Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles

Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

A 57-year-old female presents to the Emergency Department with shortness of breath and pleuritic chest pain. She has no past medical history of note and enjoys good health. Investigations reveal a non-massive pulmonary embolism. What is the recommended length of warfarinisation for this patient?

<input type="radio"/>	A. 6 weeks
<input type="radio"/>	B. 3 months
<input type="radio"/>	C. 6 months
<input type="radio"/>	D. 12 months
<input type="radio"/>	E. Life-long

There are no transient risk factors for venous thromboembolism therefore the patient should be anticoagulated for 6 months.

Recent NICE guidelines advise to 'offer a VKA\* beyond 3 months to patients with an unprovoked PE'.

\*vitamin K antagonist, i.e. warfarin

### Pulmonary embolism: management

The NICE guidelines of 2012 provided some clarity on how long patients should be anticoagulated for after a pulmonary embolism (PE). Selected points are listed below.

Low molecular weight heparin (LMWH) or fondaparinux should be given initially after a PE is diagnosed. An exception to this is for patients with a massive PE where thrombolysis is being considered. In such a situation unfractionated heparin should be used.

- a vitamin K antagonist (i.e. warfarin) should be given within 24 hours of the diagnosis
- the LMWH or fondaparinux should be continued for at least 5 days or until the international normalised ratio (INR) is 2.0 or above for at least 24 hours, whichever is longer, i.e. LMWH or fondaparinux is given at the same time as warfarin until the INR is in the therapeutic range
- warfarin should be continued for at least 3 months. At 3 months, NICE advise that clinicians should 'assess the risks and benefits of extending treatment'
- NICE advise extending warfarin beyond 3 months for patients with *unprovoked* PE. This essentially means that if there was no obvious cause or provoking factor (surgery, trauma, significant immobility) it may imply the patient has a tendency to thrombosis and should be given treatment longer than the norm of 3 months
- for patients with active cancer NICE recommend using LMWH for 6 months

### Thrombolysis

- thrombolysis is now recommended as the first-line treatment for massive PE where there is circulatory failure (e.g. hypotension). Other invasive approaches should be considered where appropriate facilities exist

Each one of the following is a known cause of occupational asthma, except:

<input type="radio"/>	A. Isocyanates
<input type="radio"/>	B. Cadmium
<input type="radio"/>	C. Soldering flux resin
<input type="radio"/>	D. Flour
<input type="radio"/>	E. Platinum salts

Next question

## Asthma: occupational

### Causes

- isocyanates - the most common cause. Example occupations include spray painting and foam moulding using adhesives
- platinum salts
- soldering flux resin
- glutaraldehyde
- flour
- epoxy resins
- proteolytic enzymes

### Diagnosis

- specific recommendations are made in the 2007 joint British Thoracic Society and SIGN guidelines
- serial measurements of peak expiratory flow are recommended at work and away from work

**Question 62 of 134**

Next

A 63-year-old man presents to the respiratory out-patients department with shortness of breath. Investigations reveal a fibrosing lung disease. A sputum sample however is positive for acid-fast bacilli. Which of the following may have predisposed him to developing tuberculosis?

<input type="radio"/>	A. Cadmium
<input type="radio"/>	B. Coal dust
<input type="radio"/>	C. White asbestos fibres
<input type="radio"/>	D. Blue asbestos fibres
<input type="radio"/>	E. Silica

Next question

**Silicosis**

Silicosis is a risk factor for developing TB (silica is toxic to macrophages)

**Features**

- fibrosing lung disease
- 'egg-shell' calcification of hilar lymph nodes

### Question 63 of 134

Next

A 52-year-old male is admitted to hospital with a temperature of 38.2 C and a 3 days history of a productive cough. He has been generally unwell for the past 10 days with flu-like symptoms. On examination blood pressure is 96/60 mmHg and the heart rate is 102 / min. Chest x-ray shows bilateral lower zone consolidation. What is the most likely causative organism?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. <i>Moraxella catarrhalis</i> |
| <input type="radio"/> | B. <i>Mycoplasma pneumoniae</i> |
| <input type="radio"/> | C. <i>Klebsiella</i>            |
| <input type="radio"/> | D. <i>Staphylococcus aureus</i> |
| <input type="radio"/> | E. <i>Chlamydia pneumoniae</i>  |

Next question

Preceding influenza predisposes to *Staphylococcus aureus* pneumonia

### Pneumonia: community-acquired

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- *Staphylococcus aureus*: commonly after the 'flu
- atypical pneumonias (e.g. Due to *Mycoplasma pneumoniae*)
- viruses

*Klebsiella pneumoniae* is classically in alcoholics

***Streptococcus pneumoniae* (pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

### Management

The British Thoracic Society published guidelines in 2009:

- low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital
- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin

**Question 64 of 134**

Next

You review a 27-year-old woman in the Emergency Department who has been admitted with an acute exacerbation of her asthma. Which one of the following features is most likely to indicate a life-threatening attack?

- ☐ A. Failure to improve after nebulised salbutamol 5mg
- ☐ B. Cannot complete sentences
- ☐ C. Oxygen saturations of 94% on room air
- ☐ D. Peak flow of 30% best or predicted
- ☐ E. Respiratory rate of 42 / min

Next question

**Asthma: acute severe**

Patients with acute severe asthma are stratified into moderate, severe or life-threatening

Moderate	Severe	Life-threatening
<ul style="list-style-type: none"><li>• PEF &gt; 50% best or predicted</li><li>• Speech normal</li><li>• RR &lt; 25 / min</li><li>• Pulse &lt; 110 bpm</li></ul>	<ul style="list-style-type: none"><li>• PEF 33 - 50% best or predicted</li><li>• Can't complete sentences</li><li>• RR &gt; 25/min</li><li>• Pulse &gt; 110 bpm</li></ul>	<ul style="list-style-type: none"><li>• PEF &lt; 33% best or predicted</li><li>• Oxygen sats &lt; 92%</li><li>• Silent chest, cyanosis or feeble respiratory effort</li><li>• Bradycardia, dysrhythmia or hypotension</li><li>• Exhaustion, confusion or coma</li></ul>

**British Thoracic Society guidelines**

- magnesium sulphate recommended as next step for patients who are not responding (e.g. 1.2 - 2g IV over 20 mins)
- little evidence to support use of IV aminophylline (although still mentioned in management plans)
- if no response consider IV salbutamol



Which of the following is not a recognised cause of pulmonary eosinophilia?

<input type="radio"/>	A. Churg-Strauss syndrome
<input type="radio"/>	B. Sulphonamides
<input type="radio"/>	C. Extrinsic allergic alveolitis
<input type="radio"/>	D. Loffler's syndrome
<input type="radio"/>	E. Allergic bronchopulmonary aspergillosis

Next question

## Pulmonary eosinophilia

Causes of pulmonary eosinophilia

- Churg-Strauss syndrome
- allergic bronchopulmonary aspergillosis (ABPA)
- Loffler's syndrome
- eosinophilic pneumonia
- hypereosinophilic syndrome
- tropical pulmonary eosinophilia
- drugs: nitrofurantoin, sulphonamides
- less common: Wegener's granulomatosis

Loffler's syndrome

- transient CXR shadowing and blood eosinophilia
- thought to be due to parasites such as *Ascaris lumbricoides* causing an alveolar reaction
- presents with a fever, cough and night sweats which often last for less than 2 weeks.
- generally a self-limiting disease

Tropical pulmonary eosinophilia

- associated with *Wuchereria bancrofti* infection

You review a 60-year-old woman in the COPD clinic. She was diagnosed with COPD four years ago and is currently maintained on a salbutamol inhaler as required and a tiotropium inhaler regularly. She has recently managed to give up smoking and her latest FEV1 was 42% of predicted. Despite her current therapy she is have frequent exacerbations. What is the most appropriate next step in her management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Salmeterol inhaler                        |
| <input type="radio"/> | B. Combined salmeterol + fluticasone inhaler |
| <input type="radio"/> | C. Long term oxygen therapy                  |
| <input type="radio"/> | D. Betamethasone inhaler                     |
| <input type="radio"/> | E. Oral aminophylline                        |

[Next question](#)

Following the 2010 NICE guidelines the next step in management would be a combined long-acting beta2-agonist (LABA) with an inhaled corticosteroid (ICS).

### COPD: stable management

NICE updated it's guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

#### General management

- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

#### Bronchodilator therapy

- a short-acting beta2-agonist (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

#### FEV1 > 50%

- long-acting beta2-agonist (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

#### FEV1 < 50%

- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness

- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline

- NICE only recommends theophylline after trials of short and long-acting bronchodilators or to people who cannot use inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics

- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale

- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD

- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

**Question 67 of 134**

Next

A 65-year-old woman with a history of chronic obstructive pulmonary disease (COPD) is admitted to the Emergency Department with breathlessness. This is her first admission with an exacerbation of COPD. Blood gases taken on room air shortly after admission are as follows:

pH	7.38
pCO <sub>2</sub>	4.9 kPa
pO <sub>2</sub>	8.8 kPa

What should her target oxygen saturations be?

- ☐ A. 94-98%
- ☐ B. 88-92%
- ☐ C. 92-94%
- ☐ D. >98%
- ☐ E. > 95% first 48 hours, > 90% rest of admission

Next question

When managing patients with COPD, once the pCO<sub>2</sub> is known to be normal the target oxygen saturations should be 94-98%.

**Oxygen therapy**

The British Thoracic Society published guidelines on emergency oxygen therapy in 2008. The following selected points are taken from the guidelines. Please see the link provided for the full guideline.

**In patients who are critically ill (anaphylaxis, shock etc) oxygen should initially be given via a reservoir mask at 15 l/min. Hypoxia kills.** The BTS guidelines specifically exclude certain conditions where the patient is acutely unwell (e.g. myocardial infarction) but stable.

**Oxygen saturation targets**

- acutely ill patients: 94-98%
- patients at risk of hypercapnia (e.g. COPD patients): 88-92% (see below)
- oxygen should be reduced in stable patients with satisfactory oxygen saturation

**Management of COPD patients**

- prior to availability of blood gases, use a 28% Venturi mask at 4 l/min and aim for an oxygen saturation of 88-92% for patients with risk factors for hypercapnia but no prior history of respiratory acidosis
- adjust target range to 94-98% if the pCO<sub>2</sub> is normal

Situations where oxygen therapy should not be used routinely if there is no evidence of hypoxia:

- myocardial infarction and acute coronary syndromes
- stroke
- obstetric emergencies
- anxiety-related hyperventilation

A 30-year-old female with a past history of asthma presents to the Emergency Department with pleuritic chest pain. Chest x-ray shows a right-sided pneumothorax with a 1.5cm rim of air and no mediastinal shift. What is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Admit for 48 hours observation  |
| <input type="radio"/> | B. Intercostal drain insertion   |
| <input type="radio"/> | C. Aspiration  |
| <input type="radio"/> | D. Discharge   |
| <input type="radio"/> | E. Immediate 14G cannula into 2nd intercostal space, mid-clavicular line |

[Next question](#)

This should be treated as a secondary pneumothorax as the patient has a history of asthma

### Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

#### Primary pneumothorax

Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails (defined as > 2 cm or still short of breath) then a chest drain should be inserted

#### Secondary pneumothorax

Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and/or the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted if the rim of air is between 1-2cm. If aspiration fails (i.e. pneumothorax is still greater than 1cm) a chest drain should be inserted. All patients should be admitted for at least 24 hours
- if the pneumothorax is less than 1cm then the BTS guidelines suggest giving oxygen and admitting for 24 hours
- regarding scuba diving, the BTS guidelines state: *'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'*

## **Iatrogenic pneumothorax**

Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

Which one of the following is least associated with bronchiectasis?

<input type="radio"/>	A. Hypogammaglobulinaemia
<input type="radio"/>	B. Allergic bronchopulmonary aspergillosis
<input type="radio"/>	C. Measles
<input type="radio"/>	D. Cystic fibrosis
<input type="radio"/>	E. Sarcoidosis

Next question

Traction bronchiectasis may be seen in some rare cases of stage IV pulmonary sarcoidosis but this is the least strong association of the five options

### Bronchiectasis: causes

Bronchiectasis describes a permanent dilatation of the airways secondary to chronic infection or inflammation. There are a wide variety of causes are listed below:

#### Causes

- post-infective: tuberculosis, measles, pertussis, pneumonia
- cystic fibrosis
- bronchial obstruction e.g. lung cancer/foreign body
- immune deficiency: selective IgA, hypogammaglobulinaemia
- allergic bronchopulmonary aspergillosis (ABPA)
- ciliary dyskinetic syndromes: Kartagener's syndrome, Young's syndrome
- yellow nail syndrome



A 43-year-old lifelong non-smoker is diagnosed as having emphysema. Further tests reveal that he has alpha-1 antitrypsin deficiency. What is the main role of alpha-1 antitrypsin in the body?

<input type="radio"/>	A. Nicotinic receptor activator
<input type="radio"/>	B. Protease inhibitor
<input type="radio"/>	C. 5-alpha-reductase inhibitor
<input type="radio"/>	D. Trypsin activator
<input type="radio"/>	E. Phosphodiesterase inhibitor

### Alpha-1 antitrypsin deficiency

Alpha-1 antitrypsin (A1AT) deficiency is a common inherited condition caused by a lack of a protease inhibitor (Pi) normally produced by the liver. The role of A1AT is to protect cells from enzymes such as neutrophil elastase.

#### Genetics

- located on chromosome 14
- inherited in an autosomal recessive / co-dominant fashion\*
- alleles classified by their electrophoretic mobility - M for normal, S for slow, and Z for very slow
- normal = PiMM
- homozygous PiSS (50% normal A1AT levels)
- homozygous PiZZ (10% normal A1AT levels)

#### Features

- patients who manifest disease usually have PiZZ genotype
- lungs: panacinar emphysema, most marked in lower lobes
- liver: cirrhosis and hepatocellular carcinoma in adults, cholestasis in children

#### Investigations

- A1AT concentrations

#### Management

- no smoking
- supportive: bronchodilators, physiotherapy
- intravenous alpha1-antitrypsin protein concentrates
- surgery: volume reduction surgery, lung transplantation

\*trusted sources are split on which is a more accurate description

A 58-year-old man is investigated for a chronic cough and is found to have lung cancer. He enquires whether it may be work related. Which one of the following is most likely to increase his risk of developing lung cancer?

<input type="radio"/>	A. Isocyanates
<input type="radio"/>	B. Soldering flux resin
<input type="radio"/>	C. Passive smoking
<input type="radio"/>	D. Coal dust
<input type="radio"/>	E. Polyvinyl chloride

[Next question](#)

Whilst many chemicals have been implicated in the development of lung cancer passive smoking is the most likely cause. Up to 15% of lung cancers in patients who do not smoke are thought to be caused by passive smoking

### Lung cancer: risk factors

#### Smoking

- increases risk of lung ca by a factor of 10

#### Other factors

- asbestos - increases risk of lung ca by a factor of 5
- arsenic
- radon
- nickel
- chromate
- aromatic hydrocarbon
- cryptogenic fibrosing alveolitis

#### Factors that are NOT related

- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a  $10 * 5 = 50$  times increased risk

**Question 72 of 134**

Next

A 54-year-old man is admitted with suspected pulmonary embolism. He has no past medical history of note. Blood pressure is 120/80 mmHg with a pulse of 90/min. The chest x-ray is normal. Following treatment with low-molecular weight heparin, what is the most appropriate initial lung imaging investigation to perform?

- ☐ A. Pulmonary angiography
- ☐ B. Echocardiogram
- ☐ C. MRI thorax
- ☐ D. Ventilation-perfusion scan
- ☐ E. Computed tomographic pulmonary angiography

Next question

CTPA is the first line investigation for PE according to current BTS guidelines

This is a difficult question to answer as both computed tomographic pulmonary angiography (CTPA) and ventilation-perfusion scanning are commonly used in UK clinical practice. The 2003 British Thoracic Society (BTS) guidelines, however, recommended that CTPA is now used as the initial lung imaging modality of choice. Pulmonary angiography is of course the 'gold standard' but this is not what the question asks for

**Pulmonary embolism: investigation****2012 NICE guidelines**

All patients with symptoms or signs suggestive of a PE should have a history taken, examination performed and a chest x-ray to exclude other pathology.

If a PE is still suspected a two-level PE Wells score should be performed:

Clinical feature	Points
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3
An alternative diagnosis is less likely than PE	3
Heart rate > 100 beats per minute	1.5
Immobilisation for more than 3 days or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Haemoptysis	1
Malignancy (on treatment, treated in the last 6 months, or palliative)	1

Clinical probability simplified scores

- PE likely - more than 4 points

- PE unlikely - 4 points or less

If a PE is 'likely' (more than 4 points) arrange an immediate computed tomography pulmonary angiogram (CTPA). If there is a delay in getting the CTPA then give low-molecular weight heparin until the scan is performed.

If a PE is 'unlikely' (4 points or less) arranged a D-dimer test. If this is positive arrange an immediate computed tomography pulmonary angiogram (CTPA). If there is a delay in getting the CTPA then give low-molecular weight heparin until the scan is performed.

If the patient has an allergy to contrast media or renal impairment a V/Q scan should be used instead of a CTPA.

### **CTPA or V/Q scan?**

The British Thoracic Society (BTS) published guidelines back in 2003 on the management of patients with suspected pulmonary embolism (PE). Key points from the guidelines include:

- computed tomographic pulmonary angiography (CTPA) is now the recommended initial lung-imaging modality for non-massive PE. Advantages compared to V/Q scans include speed, easier to perform out-of-hours, a reduced need for further imaging and the possibility of providing an alternative diagnosis if PE is excluded
- if the CTPA is negative then patients do not need further investigations or treatment for PE
- ventilation-perfusion scanning may be used initially if appropriate facilities exist, the chest x-ray is normal, and there is no significant symptomatic concurrent cardiopulmonary disease

### **Some other points**

#### **D-dimers**

- sensitivity = 95-98%, but poor specificity

#### **ECG**

- the classic ECG changes seen in PE are a large S wave in lead I, a large Q wave in lead III and an inverted T wave in lead III - 'S1Q3T3'. However this change is seen in no more than 20% of patients
- right bundle branch block and right axis deviation are also associated with PE
- sinus tachycardia may also be seen

#### **V/Q scan**

- sensitivity = 98%; specificity = 40% - high negative predictive value, i.e. if normal virtually excludes PE
- other causes of mismatch in V/Q include old pulmonary embolisms, AV malformations, vasculitis, previous radiotherapy
- COPD gives matched defects

## CTPA

- peripheral emboli affecting subsegmental arteries may be missed

## Pulmonary angiography

- the gold standard
- significant complication rate compared to other investigations

**Question 73 of 134**

Next

A 39-year-old man presents with shortness of breath following one week of flu-like symptoms. He also has a non-productive cough but no chest pain. A chest x-ray shows bilateral consolidation and examination reveals erythematous lesions on his limbs and trunk. Which one of the following investigations is most likely to be diagnostic?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Cold agglutins                 |
| <input type="radio"/> | B. Sputum culture                 |
| <input type="radio"/> | C. Urinary antigen for Legionella |
| <input type="radio"/> | D. Serology for Mycoplasma        |
| <input type="radio"/> | E. Blood culture                  |

Next question

Mycoplasma? - serology is diagnostic

The flu-like symptoms, bilateral consolidation and erythema multiforme point to a diagnosis of Mycoplasma. The most appropriate diagnostic test is Mycoplasma serology

***Mycoplasma pneumoniae***

*Mycoplasma pneumoniae* is a cause of atypical pneumonia which often affects younger patients. It is associated with a number of characteristic complications such as erythema multiforme and cold autoimmune haemolytic anaemia. Epidemics of *Mycoplasma pneumoniae* classically occur every 4 years. It is important to recognise atypical pneumonias as they may not respond to penicillins or cephalosporins

**Features**

- the disease typically has a prolonged and gradual onset
- flu-like symptoms classically precede a dry cough
- bilateral consolidation on x-ray
- complications may occur as below

**Complications**

- cold agglutins (IgM) may cause an haemolytic anaemia, thrombocytopenia
- erythema multiforme, erythema nodosum
- meningoencephalitis, Guillain-Barre syndrome
- bullous myringitis: painful vesicles on the tympanic membrane
- pericarditis/myocarditis
- gastrointestinal: hepatitis, pancreatitis
- renal: acute glomerulonephritis

## Diagnosis

- Mycoplasma serology

## Management

- erythromycin/clarithromycin
- tetracyclines such as doxycycline are an alternative

Which type of hypersensitivity reaction predominates in the acute phase of extrinsic allergic alveolitis?

- |                       |             |
|-----------------------|-------------|
| <input type="radio"/> | A. Type I   |
| <input type="radio"/> | B. Type II  |
| <input type="radio"/> | C. Type III |
| <input type="radio"/> | D. Type IV  |
| <input type="radio"/> | E. Type V   |

Next question

Although it is known that the pathogenesis of extrinsic allergic alveolitis involves a type IV (delayed) hypersensitivity reaction, a type III hypersensitivity reaction is thought to predominate, especially in the acute phase

### Extrinsic allergic alveolitis

Extrinsic allergic alveolitis (EAA, also known as hypersensitivity pneumonitis) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles. It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase.

#### Examples

- bird fanciers' lung: avian proteins
- farmers lung: spores of *Saccharopolyspora rectivirgula* (formerly *Micropolyspora faeni*)
- malt workers' lung: *Aspergillus clavatus*
- mushroom workers' lung: thermophilic actinomycetes\*

#### Presentation

- acute: occur 4-8 hrs after exposure, SOB, dry cough, fever
- chronic

#### Investigation

- chest x-ray: upper lobe fibrosis
- bronchoalveolar lavage: lymphocytosis
- blood: NO eosinophilia

\*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as *Micropolyspora faeni*



A 60-year-old woman who has recently been diagnosed with chronic obstructive pulmonary disease (COPD) presents for review. She is still occasionally breathless despite using a short-acting muscarinic antagonist (SAMA) as required. Her FEV1 is 45% of predicted and she has managed to stop smoking. Of the following options, which one is the most appropriate next step in management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Switch to a combined short-acting beta2-agonist and muscarinic antagonist inhaler (e.g. Combivent) |
| <input type="radio"/> | B. Long-acting beta2-agonist  |
| <input type="radio"/> | C. Long-acting beta2-agonist + inhaled corticosteroid (ICS) in a combination inhaler                  |
| <input type="radio"/> | D. Inhaled corticosteroid   |
| <input type="radio"/> | E. Use the SAMA regularly (e.g. 2 puffs qds)  |

[Next question](#)

Another option here is a long-acting muscarinic antagonist (LAMA), for example tiotropium. Please see the 2010 NICE guidelines for more details.

### COPD: stable management

NICE updated its guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

#### General management

- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

#### Bronchodilator therapy

- a short-acting beta2-agonist (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

#### FEV1 > 50%

- long-acting beta2-agonist (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

#### FEV1 < 50%

- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:

- LAMA

For patients with persistent exacerbations or breathlessness

- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline

- NICE only recommends theophylline after trials of short and long-acting bronchodilators or to people who cannot use inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics

- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale

- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD

- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

**Question 76 of 134**

Next

A 54-year-old woman with chronic obstructive pulmonary disease (COPD) is prescribed an inhaled corticosteroid. What is the main therapeutic benefit of inhaled corticosteroids in patients with COPD?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. Reduced severity of exacerbations  |
| <input type="radio"/> | B. Improved all cause mortality       |
| <input type="radio"/> | C. Reduced use of bronchodilators     |
| <input type="radio"/> | D. Slows decline in FEV1              |
| <input type="radio"/> | E. Reduced frequency of exacerbations |

Next question

COPD - reason for using inhaled corticosteroids - reduced exacerbations

**COPD: stable management**

NICE updated its guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

**General management**

- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

**Bronchodilator therapy**

- a short-acting beta2-agonist (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

**FEV1 > 50%**

- long-acting beta2-agonist (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

**FEV1 < 50%**

- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness

- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline

- NICE only recommends theophylline after trials of short and long-acting bronchodilators or to people who cannot use inhaled therapy
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Mucolytics

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- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD

- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

A 55-year-old man is diagnosed with non-small cell lung cancer. Which one of the following is a contraindication to surgery?

<input type="radio"/>	A. Pleural effusion
<input type="radio"/>	B. FEV1 of 1.3 litres
<input type="radio"/>	C. Continuation of smoking
<input type="radio"/>	D. Hypercalcaemia
<input type="radio"/>	E. Stage T2N1

[Next question](#)

Contraindications to lung cancer surgery include SVC obstruction, FEV < 1.5, MALIGNANT pleural effusion, and vocal cord paralysis

### Lung cancer: non-small cell management

#### Management

- only 20% suitable for surgery
- mediastinoscopy performed prior to surgery as CT does not always show mediastinal lymph node involvement
- curative or palliative radiotherapy
- poor response to chemotherapy

#### Surgery contraindications

- assess general health
- stage IIIb or IV (i.e. metastases present)
- FEV1 < 1.5 litres is considered a general cut-off point\*
- malignant pleural effusion
- tumour near hilum
- vocal cord paralysis
- SVC obstruction

\* However if FEV1 < 1.5 for lobectomy or < 2.0 for pneumonectomy then some authorities advocate further lung function tests as operations may still go ahead based on the results

**Question 78 of 134**

Next

A 31-year-old woman is investigated for lethargy, arthralgia and cough. Over the past few weeks she has also developed painful erythematous nodules on both shins. Respiratory examination is normal. A chest x-ray is performed which is reported as follows:

Bilateral mediastinal nodal enlargement. No evidence of lung parenchymal disease. Normal cardiac size.

Given the likely diagnosis, what is the most appropriate course of action?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Inhaled corticosteroids |
| <input type="radio"/> | B. Oral cyclophosphamide   |
| <input type="radio"/> | C. Oral corticosteroids    |
| <input type="radio"/> | D. Oral methotrexate       |
| <input type="radio"/> | E. Observation             |

Next question

This patient has sarcoidosis as evidenced by the erythema nodosum and bilateral hilar lymphadenopathy. The chest x-ray is consistent with stage 1 changes. There are no indications here for steroid therapy so observation is the most appropriate action.

**Sarcoidosis: management**

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas. It is more common in young adults and in people of African descent

Indications for steroids

- hypercalcaemia
- worsening lung function
- eye, heart or neuro involvement

A newborn female baby is diagnosed with cystic fibrosis following an episode of meconium ileus shortly after birth. Which one of the following is least likely to occur as a consequence of her underlying diagnosis?

<input type="radio"/>	A. Delayed puberty
<input type="radio"/>	B. Nasal polyps
<input type="radio"/>	C. Diabetes mellitus
<input type="radio"/>	D. Rectal prolapse
<input type="radio"/>	E. Arthropathy

[Next question](#)

Arthropathy is not a common feature of cystic fibrosis

### Cystic fibrosis: features

#### Presenting features

- neonatal period (around 20%): meconium ileus, less commonly prolonged jaundice
- recurrent chest infections (40%)
- malabsorption (30%): steatorrhoea, failure to thrive
- other features (10%): liver disease

#### Other features of cystic fibrosis

- short stature
- diabetes mellitus
- delayed puberty
- rectal prolapse (due to bulky stools)
- nasal polyps
- male infertility, female subfertility

A 23-year-old female who is 28 weeks pregnant presents with shortness-of-breath and right-sided pleuritic chest pain. A diagnosis of pulmonary embolism is suspected. Which one of the following statements regarding the appropriate management is incorrect?

- ☐ A. Chest x-ray should be performed
- ☐ B. Positive compression duplex Doppler may negate the need for further investigation
- ☐ C. Ventilation-perfusion scanning exposes the fetus to less radiation than computed tomographic pulmonary angiography
- ☐ D. D-dimer levels are of no use
- ☐ E. Computed tomographic pulmonary angiography increases the lifetime risk of breast cancer in the pregnant women

[Next question](#)

### Pregnancy: DVT/PE investigation

Guidelines were updated in 2010 by the Royal College of Obstetricians. Key points include:

- chest x-ray should be performed in all patients
- compression duplex Doppler should be performed if the chest x-ray is normal - this may provide indirect evidence of a pulmonary embolism and negate the need for further radiation exposure
- the decision to perform a V/Q or CTPA should be taken at a local level after discussion with the patient and radiologist

### Comparing CTPA to V/Q scanning in pregnancy

CTPA	V/Q scanning
CTPA slightly increases the lifetime risk of <b>maternal breast cancer</b> (increased by up to 13.6%, background risk of 1/200 for study population). Pregnancy makes breast tissue particularly sensitive to the effects of radiation	V/Q scanning carries a slightly increased risk of <b>childhood cancer</b> compared with CTPA (1/280,000 versus less than 1/1,000,000)

D-dimer is of limited use in the investigation of thromboembolism as it often raised in pregnancy.



A 65-year-old man with a history of Parkinson's disease is referred to the respiratory clinic with shortness of breath. He has never smoked. Spirometry is performed:

	Percentage predicted
FEV1	71%
FVC	74%

Which one of the following drugs is most likely to be responsible?

- ☐ A. Levodopa
- ☐ B. Entacapone
- ☐ C. Ropinirole
- ☐ D. Selegiline
- ☐ E. Pergolide

Next question

This patient has developed pulmonary fibrosis (explaining the restrictive picture on spirometry) secondary to pergolide therapy

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine

- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

#### Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

#### COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

#### Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benzotropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Which one of the following is least associated with the development of COPD?

<input type="radio"/>	A. Cadmium exposure
<input type="radio"/>	B. Smoking
<input type="radio"/>	C. Coal dust
<input type="radio"/>	D. Isocyanates
<input type="radio"/>	E. Alpha-1 antitrypsin deficiency

Next question

Isocyanates are more associated with occupational asthma

### COPD: causes

Smoking!

Alpha-1 antitrypsin deficiency

Other causes

- cadmium (used in smelting)
- coal
- cotton
- cement
- grain

A 33-year-old man is seen in the respiratory clinic. He was referred with poorly control asthma and has recently had salmeterol added in addition to beclometasone dipropionate inhaler 200mcg bd and salbutamol prn. There has unfortunately been no response to adding the salmeterol. What is the most appropriate action?

- ☐ A. Stop salmeterol + trial of leukotriene receptor antagonist
- ☐ B. Continue salmeterol + increase beclometasone dipropionate inhaler to 400mcg bd
- ☐ C. Continue salmeterol + trial of leukotriene receptor antagonist
- ☐ D. Stop salmeterol + trial of oral theophylline
- ☐ E. Stop salmeterol + increase beclometasone dipropionate inhaler to 400mcg bd

[Next question](#)

### Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

<b>Step 1</b>	Inhaled short-acting B2 agonist as required
<b>Step 2</b>	Add inhaled steroid at 200-800 mcg/day*  400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
<b>Step 3</b>	1. Add inhaled long-acting B2 agonist (LABA)  2. Assess control of asthma: <ul style="list-style-type: none"> <li>• good response to LABA - continue LABA</li> <li>• benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose)</li> <li>• no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline</li> </ul>
<b>Step 4</b>	Consider trials of: <ul style="list-style-type: none"> <li>• increasing inhaled steroid up to 2000 mcg/day*</li> <li>• addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet</li> </ul>
<b>Step 5</b>	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets  Maintain high dose inhaled steroid at 2000 mcg/day*  Refer patient for specialist care

\*beclometasone dipropionate or equivalent

## Additional notes

### Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone

Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles

Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

What is the first line treatment in allergic bronchopulmonary aspergillosis?

<input type="radio"/>	A. Itraconazole
<input type="radio"/>	B. Nebulised pentamidine
<input type="radio"/>	C. Fluconazole
<input type="radio"/>	D. Cyclophosphamide
<input type="radio"/>	E. Prednisolone

Next question

### Allergic bronchopulmonary aspergillosis

Allergic bronchopulmonary aspergillosis results from an allergy to *Aspergillus* spores. In the exam questions often give a history of bronchiectasis and eosinophilia.

#### Features

- bronchoconstriction: wheeze, cough, dyspnoea
- bronchiectasis (proximal)

#### Investigations

- eosinophilia
- flitting CXR changes
- positive radioallergosorbent (RAST) test to *Aspergillus*
- positive IgG precipitins (not as positive as in aspergilloma)
- raised IgE

#### Management

- steroids
- itraconazole is sometimes introduced as a second line agent

**Question 85 of 134**

Next

A 45-year-old female with a 30 pack-year history of smoking is admitted to the Emergency Department with shortness of breath. Arterial blood gases taken on room air are as follows:

pH	7.49
pCO <sub>2</sub>	2.9 kPa
pO <sub>2</sub>	8.8 kPa

Which one of the following is the most likely diagnosis?

<input type="radio"/>	A. Salicylate overdose
<input type="radio"/>	B. Chronic obstructive pulmonary disease
<input type="radio"/>	C. Pulmonary embolism
<input type="radio"/>	D. Vomiting
<input type="radio"/>	E. Anxiety

Next question

Pulmonary embolism needs to be excluded. Even with a significant smoking history a reduced pO<sub>2</sub> should not be attributed to anxiety. A salicylate overdose would not account for a reduced pO<sub>2</sub>, unless it is severe enough to have caused pulmonary oedema. This option is much less likely than a pulmonary embolism

**Respiratory alkalosis**

Common causes

- anxiety leading to hyperventilation
- pulmonary embolism
- salicylate poisoning\*
- CNS disorders: stroke, subarachnoid haemorrhage, encephalitis
- altitude
- pregnancy

\*salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis

Which one of the following interventions is most likely to increase survival in patients with COPD?

<input type="radio"/>	A. Home nebulisers
<input type="radio"/>	B. Tiotropium inhaler
<input type="radio"/>	C. Long-term steroid therapy
<input checked="" type="radio"/>	D. Smoking cessation
<input type="radio"/>	E. Long-term oxygen therapy

Next question

Whilst long-term oxygen therapy may increase survival in hypoxic patients, smoking cessation is the single most important intervention in patients with COPD

### COPD: stable management

NICE updated its guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

#### General management

- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

#### Bronchodilator therapy

- a short-acting beta2-agonist (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

#### FEV1 > 50%

- long-acting beta2-agonist (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

#### FEV1 < 50%

- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness



- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

#### Oral theophylline

- NICE only recommends theophylline after trials of short and long-acting bronchodilators or to people who cannot use inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

#### Mucolytics

- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

#### Cor pulmonale

- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

#### Factors which may improve survival in patients with stable COPD

- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

A 67-year-old man is referred to the respiratory clinic. He has a past history of tuberculosis as a child but is otherwise normally fit and well. Over the past two months he has had a cough, lost one stone in weight and had four episodes of haemoptysis. A chest x-ray shows a solid mass occupying the right upper zone. Investigation results include the following:

Aspergillus precipitin antibody	Positive
---------------------------------	----------

What is the most likely diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Lung abscess                            |
| <input type="radio"/> | B. Invasive aspergillosis                  |
| <input type="radio"/> | C. Aspergilloma                            |
| <input type="radio"/> | D. Reactivation of primary tuberculosis    |
| <input type="radio"/> | E. Allergic bronchopulmonary aspergillosis |

Next question

## Aspergilloma

An aspergilloma is a fungus ball which often colonises an existing lung cavity (e.g. secondary to TB, lung cancer or cystic fibrosis)

Usually asymptomatic but features may include

- cough
- haemoptysis (may be severe)

Investigations

- CXR containing a rounded opacity
- high titres Aspergillus precipitins

Which one of the following is the most common type of lung cancer in the UK?

<input type="radio"/>	A. Small cell
<input type="radio"/>	B. Squamous cell
<input type="radio"/>	C. Adenocarcinoma
<input type="radio"/>	D. Large cell
<input type="radio"/>	E. Carcinoid

Next question

Tricky question. It is well known that the incidence of adenocarcinoma is rising in comparison to the other types of non-small cell lung cancer. Indeed, adenocarcinoma is now the most common type of lung cancer in the USA. In the UK however squamous cell cancer remains the most common subtype

#### Reference

Janssen-Heijnen, M.L. and J.W. Coebergh, The changing epidemiology of lung cancer in Europe. Lung Cancer, 2003. 41(3)

#### Lung cancer: types

##### Lung cancer

- squamous: c. 35%
- adenocarcinoma: c. 30%
- small (oat) cell: c. 15%
- large cell: c. 10%
- other c. 5%

##### Other tumours

- alveolar cell carcinoma: not related to smoking, ++sputum
- bronchial adenoma: mostly carcinoid

A 19-year-old male with no past medical history presents to the Emergency Department with anterior chest pain and shortness of breath. Blood pressure is 110/80 mmHg and his pulse is 84 bpm. The chest x-ray is reported as showing a 50% pneumothorax with no mid-line shift. What is the most appropriate management?

<input type="radio"/>	A. Intercostal drain insertion
<input type="radio"/>	B. Immediate 14G cannula into 2nd intercostal space, mid-clavicular line
<input type="radio"/>	C. Discharge
<input type="radio"/>	D. Admit for 48 hours observation and repeat chest x-ray
<input type="radio"/>	E. Aspiration

Next question

Questions may occasionally quote a percentage figure rather than 'rim size'. A 50% pneumothorax is likely to have a rim of > 3cm. Please see the American Journal of Radiology link for more information on the relationship between rim size and percentage.

## Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

### Primary pneumothorax

Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails (defined as > 2 cm or still short of breath) then a chest drain should be inserted

### Secondary pneumothorax

Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and/or the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted if the rim of air is between 1-2cm. If aspiration fails (i.e. pneumothorax is still greater than 1cm) a chest drain should be inserted. All patients should be admitted for at least 24 hours
- if the pneumothorax is less than 1cm then the BTS guidelines suggest giving oxygen and admitting for 24 hours

- regarding scuba diving, the BTS guidelines state: *'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'*

## **Iatrogenic pneumothorax**

Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

A 54-year-old woman with a 30-pack-year history of smoking presents due to increasing breathlessness. A diagnosis of chronic obstructive pulmonary disease (COPD) is suspected. Which of the following diagnostic criteria should be used when assessing a patient with suspected COPD?

- ☐ A.  $FEV_1 > 70\%$  of predicted value +  $FEV_1/FVC < 60\%$
- ☐ B.  $FEV_1/FVC < 70\%$  + symptoms suggestive of COPD
- ☐ C.  $FEV_1 < 70\%$  of predicted value +  $FEV_1/FVC < 70\%$
- ☐ D.  $FEV_1 < 80\%$  of predicted value +  $FEV_1/FVC < 60\%$
- ☐ E.  $FEV_1 < 70\%$  of predicted value +  $FEV_1/FVC > 70\%$

Next question

Please see the 2010 NICE guidelines for further details. Patients can now be diagnosed with 'mild' COPD if their  $FEV_1$  predicted is  $> 80\%$  if they have symptoms suggestive of COPD.

### COPD: investigation and diagnosis

NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are smokers or ex-smokers and have symptoms such as exertional breathlessness, chronic cough or regular sputum production.

The following investigations are recommended in patients with suspected COPD:

- post-bronchodilator spirometry to demonstrate airflow obstruction:  $FEV_1/FVC$  ratio less than 70%
- chest x-ray: hyperinflation, bullae, flat hemidiaphragm. Also important to exclude lung cancer
- full blood count: exclude secondary polycythaemia
- body mass index (BMI) calculation

The severity of COPD is categorised using the  $FEV_1^*$ :

Post-bronchodilator $FEV_1/FVC$	$FEV_1$ (of predicted)	Severity
$< 0.7$	$> 80\%$	Stage 1 - Mild**
$< 0.7$	50-79%	Stage 2 - Moderate
$< 0.7$	30-49%	Stage 3 - Severe
$< 0.7$	$< 30\%$	Stage 4 - Very severe

Measuring peak expiratory flow is of limited value in COPD, as it may underestimate the degree of airflow obstruction.

\*note that the grading system has changed following the 2010 NICE guidelines. If the  $FEV_1$  is greater than 80% predicted but the post-bronchodilator  $FEV_1/FVC$  is  $< 0.7$  then this is classified as Stage 1 - mild

\*\*symptoms should be present to diagnose COPD in these patients

Which one of the following is responsible for malt workers' lung?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. <i>Aspergillus clavatus</i>       |
| <input type="radio"/> | B. Avian proteins                    |
| <input type="radio"/> | C. <i>Mycobacterium avium</i>        |
| <input type="radio"/> | D. <i>Thermoactinomyces candidus</i> |
| <input type="radio"/> | E. <i>Micropolyspora faeni</i>       |

Next question

Aspergillus clavatus causes malt workers' lung, a type of EAA

### Extrinsic allergic alveolitis

Extrinsic allergic alveolitis (EAA, also known as hypersensitivity pneumonitis) is a condition caused by hypersensitivity induced lung damage due to a variety of inhaled organic particles. It is thought to be largely caused by immune-complex mediated tissue damage (type III hypersensitivity) although delayed hypersensitivity (type IV) is also thought to play a role in EAA, especially in the chronic phase.

#### Examples

- bird fanciers' lung: avian proteins
- farmers lung: spores of *Saccharopolyspora rectivirgula* (formerly *Micropolyspora faeni*)
- malt workers' lung: *Aspergillus clavatus*
- mushroom workers' lung: thermophilic actinomycetes\*

#### Presentation

- acute: occur 4-8 hrs after exposure, SOB, dry cough, fever
- chronic

#### Investigation

- chest x-ray: upper lobe fibrosis
- bronchoalveolar lavage: lymphocytosis
- blood: NO eosinophilia

\*here the terminology is slightly confusing as thermophilic actinomycetes is an umbrella term covering strains such as *Micropolyspora faeni*

A 29-year-old man with HIV is admitted with shortness of breath. He has recently emigrated from South Africa and has only just started taking anti-retroviral medication. Auscultation of his chest is unremarkable although chest x-ray shows bilateral pulmonary interstitial shadowing. What is the investigation of choice?

<input type="radio"/>	A. Bronchoalveolar lavage
<input type="radio"/>	B. CT thorax
<input type="radio"/>	C. Transbronchial biopsy
<input type="radio"/>	D. Sputum culture
<input type="radio"/>	E. Blood culture

[Next question](#)

This man likely has *Pneumocystis carinii* pneumonia. Definitive diagnosis is by bronchial alveolar lavage with silver staining

#### HIV: *Pneumocystis jiroveci* pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as *Pneumocystis jiroveci*, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- *Pneumocystis jiroveci* is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count  $< 200/\text{mm}^3$  should receive PCP prophylaxis

#### Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Extrapulmonary manifestations are rare (1-2% of cases), may cause

- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

#### Investigation



- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal
- exercise-induced desaturation
- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain)

## Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if  $pO_2 < 9.3\text{kPa}$  then steroids reduce risk of respiratory failure by 50% and death by a third)

**Question 93 of 134**

Next

A 65-year-old man is admitted with fever and dyspnoea. A chest x-ray shows extensive shadowing in the right lower zone. Which one of the following is associated with a poor prognosis in patients with community-acquired pneumonia?

<input type="radio"/>	A. Diastolic blood pressure 65 mmHg
<input type="radio"/>	B. Sodium 131 mmol/l
<input type="radio"/>	C. Urea 12 mmol/l
<input type="radio"/>	D. White blood cell $27 \times 10^9/l$
<input type="radio"/>	E. Respiratory rate 25/min

Next question

**Pneumonia: prognostic factors**

CURB-65 criteria of severe pneumonia

- Confusion (abbreviated mental test score  $\leq 8/10$ )
- Urea  $> 7$  mmol/L
- Respiratory rate  $\geq 30$  / min
- BP: systolic  $\leq 90$  or diastolic  $\leq 60$  mmHg
- age  $\geq 65$  years

Patients with 3 or more (out of 5) of the above criteria are regarded as having a severe pneumonia

Other factors associated with a poor prognosis include:

- presence of coexisting disease
- hypoxaemia ( $pO_2 < 8$  kPa) independent of  $FiO_2$

**Question 94 of 134**

Next

A 29-year-old man who is being investigated for haemoptysis and a chronic cough has a blood screen:

Hb	12.9 g/dl
Plt	$248 \times 10^9/l$
WBC	$5.4 \times 10^9/l$
ESR	11 mm/hr
Na <sup>+</sup>	138 mmol/l
K <sup>+</sup>	5.0 mmol/l
Bicarbonate	19 mmol/l
Urea	14.0 mmol/l
Creatinine	178 $\mu$ mol/l

Urine dipstick shows blood ++. What is the most likely diagnosis?

- ☐ A. Wegener's granulomatosis
- ☐ B. Lung cancer with renal metastases
- ☐ C. Churg-Strauss syndrome
- ☐ D. Renal cancer with lung metastases
- ☐ E. Goodpasture's syndrome

Next question

The age of the patient and normal ESR point to a diagnosis of Goodpasture's syndrome.

**Goodpasture's syndrome**

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Goodpasture's syndrome is more common in men (sex ratio 2:1) and has a bimodal age distribution (peaks in 20-30 and 60-70 age bracket). It is associated with HLA DR2.

**Features**

- pulmonary haemorrhage
- followed by rapidly progressive glomerulonephritis

Factors which increase likelihood of pulmonary haemorrhage

- smoking
- lower respiratory tract infection

- pulmonary oedema
- inhalation of hydrocarbons
- young males

### Investigations

- renal biopsy: linear IgG deposits along basement membrane
- raised transfer factor secondary to pulmonary haemorrhages

### Management

- plasma exchange
- steroids
- cyclophosphamide

A 38-year-old man is reviewed in the respiratory clinic complaining of episodic wheezing whilst playing rugby. There is no history of cough, atopy or smoking. He is generally fit and well and has no past medical history of note. Clinical examination is unremarkable. Following history and examination it is thought he has an intermediate probability of asthma. Which one of the following is the most appropriate next investigation?

- ☐ A. Spirometry
- ☐ B. Serial peak expiratory flow measurements
- ☐ C. Histamine stimulation test
- ☐ D. Methacholine stimulation test
- ☐ E. A trial of inhaled steroids with FEV1 measurements before and after

Next question

Asthma - intermediate probability - do spirometry first-line

If the FEV1/FVC < 0.7 then a trial of treatment is appropriate. Otherwise further investigations should be performed

### Asthma: diagnosis in adults

The 2008 British Thoracic Society guidelines marked a subtle change in the approach to diagnosing asthma. This approach is supported in the updated 2011 guidelines. It suggests dividing patients into a high, intermediate and low probability of having asthma based on the presence or absence of typical symptoms. A list can be found in the external link but include typical symptoms such as wheeze, nocturnal cough etc

Example of features used to assess asthma (not complete, please see link)

Increase possibility of asthma	Decrease possibility of asthma
<ul style="list-style-type: none"> <li>• Wheeze, breathlessness, chest tightness and cough, worse at night/early morning</li> <li>• History of atopic disorder</li> <li>• Wheeze heard on auscultation</li> <li>• Unexplained peripheral blood eosinophilia</li> </ul>	<ul style="list-style-type: none"> <li>• Prominent dizziness, light-headedness, peripheral tingling</li> <li>• Chronic productive cough in the absence of wheeze or breathlessness</li> <li>• Repeatedly normal physical examination</li> <li>• Significant smoking history (i.e. &gt; 20 pack-years)</li> <li>• Normal PEF or spirometry when symptomatic</li> </ul>

Management is based on this assessment:

- high probability: trial of treatment
- intermediate probability: see below
- low probability: investigate/treat other condition

For patients with an intermediate probability of asthma further investigations are suggested. The guidelines state that spirometry is the preferred initial test:

- FEV1/FVC < 0.7: trial of treatment
- FEV1/FVC > 0.7: further investigation/consider referral

Recent studies have shown the limited value of other 'objective' tests. It is now recognised that in patients with normal or near-normal pre-treatment lung function there is little room for measurable improvement in FEV1 or peak flow.

A > 400 ml improvement in FEV1 is considered significant

- before and after 400 mcg inhaled salbutamol in patients with diagnostic uncertainty and airflow obstruction present at the time of assessment
- if there is an incomplete response to inhaled salbutamol, after either inhaled corticosteroids (200 mcg twice daily beclometasone equivalent for 6-8 weeks) or oral prednisolone (30 mg once daily for 14 days)

It is now advised to interpret peak flow variability with caution due to the poor sensitivity of the test

- diurnal variation % =  $[(\text{Highest} - \text{Lowest PEFr}) / \text{Highest PEFr}] \times 100$
- assessment should be made over 2 weeks
- greater than 20% diurnal variation is considered significant

A 56-year-old man is admitted with type II respiratory failure secondary to COPD but fails to respond to maximal medical therapy. It is decided that a trial of non-invasive ventilation in the form of bi-level pressure support should be given. What are the most appropriate initial settings for the ventilator?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. IPAP = 10 cm H <sub>2</sub> O; EPAP = 5 cm H <sub>2</sub> O  |
| <input type="radio"/> | B. IPAP = 15 cm H <sub>2</sub> O; EPAP = 15 cm H <sub>2</sub> O |
| <input type="radio"/> | C. IPAP = 50 cm H <sub>2</sub> O; EPAP = 20 cm H <sub>2</sub> O |
| <input type="radio"/> | D. IPAP = 20 cm H <sub>2</sub> O; EPAP = 50 cm H <sub>2</sub> O |
| <input type="radio"/> | E. IPAP = 5 cm H <sub>2</sub> O; EPAP = 12 cm H <sub>2</sub> O  |

[Next question](#)

The 2008 Royal College of Physicians guidelines recommend an initial IPAP of 10 cm H<sub>2</sub>O. The 2002 British Thoracic Society guidelines had previously advocated starting at 12-15 cm H<sub>2</sub>O

### Non-invasive ventilation

The British Thoracic Society (BTS) published guidelines in 2002 on the use of non-invasive ventilation in acute respiratory failure. Following these the Royal College of Physicians published guidelines in 2008.

Non-invasive ventilation - key indications

- COPD with respiratory acidosis pH 7.25-7.35
- type II respiratory failure secondary to chest wall deformity, neuromuscular disease or obstructive sleep apnoea
- cardiogenic pulmonary oedema unresponsive to CPAP
- weaning from tracheal intubation

Recommended initial settings for bi-level pressure support in COPD

- Expiratory Positive Airway Pressure (EPAP): 4-5 cm H<sub>2</sub>O
- Inspiratory Positive Airway Pressure (IPAP): RCP advocate 10 cm H<sub>2</sub>O whilst BTS suggest 12-15 cm H<sub>2</sub>O
- back up rate: 15 breaths/min
- back up inspiration:expiration ratio: 1:3

A 45-year-old woman who is known to have systemic lupus erythematosus (SLE) is referred to the respiratory clinic with increased shortness-of-breath. A number of investigations are ordered including transfer factor of the lung for carbon monoxide (TLCO), which is elevated. Which one of the following respiratory complications of SLE is associated with this finding?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. Acute lupus pneumonitis     |
| <input type="radio"/> | B. Pulmonary hypertension      |
| <input type="radio"/> | C. Alveolar haemorrhage        |
| <input type="radio"/> | D. Respiratory muscle weakness |
| <input type="radio"/> | E. Pulmonary embolism          |

[Next question](#)

### Transfer factor

The transfer factor describes the rate at which a gas will diffuse from alveoli into blood. Carbon monoxide is used to test the rate of diffusion. Results may be given as the total gas transfer (TLCO) or that corrected for lung volume (transfer coefficient, KCO)

Causes of a raised TLCO	Causes of a lower TLCO
<ul style="list-style-type: none"> <li>• asthma</li> <li>• pulmonary haemorrhage (Wegener's, Goodpasture's)</li> <li>• left-to-right cardiac shunts</li> <li>• polycythaemia</li> <li>• hyperkinetic states</li> <li>• male gender, exercise</li> </ul>	<ul style="list-style-type: none"> <li>• pulmonary fibrosis</li> <li>• pneumonia</li> <li>• pulmonary emboli</li> <li>• pulmonary oedema</li> <li>• emphysema</li> <li>• anaemia</li> <li>• low cardiac output</li> </ul>

KCO also tends to increase with age. Some conditions may cause an increased KCO with a normal or reduced TLCO

- pneumonectomy/lobectomy
- scoliosis/kyphosis
- neuromuscular weakness
- ankylosis of costovertebral joints e.g. ankylosing spondylitis



A 77-year-old man with a history of type 2 diabetes mellitus is admitted to hospital with worsening shortness-of-breath. He started a course of amoxicillin given by his GP 5 days ago. On examination blood pressure is 88/60 mmHg with a respiratory rate of 36 / min. A chest x-ray reveals left lower lobe consolidation. Arterial blood gases on air are as follows:

pH	7.37
pCO <sub>2</sub>	5.5 kPa
pO <sub>2</sub>	9.1 kPa

What is the most suitable antibiotic therapy?

- ☐ A. Oral amoxicillin + erythromycin
- ☐ B. Intravenous ceftriaxone
- ☐ C. Intravenous co-amoxiclav + clarithromycin
- ☐ D. Intravenous vancomycin + clarithromycin
- ☐ E. Oral co-amoxiclav + erythromycin

Next question

This patient has a severe pneumonia as the CURB score is 3. He should therefore be treated with a combination of intravenous antibiotics as recommended by the British Thoracic Society guidelines.

### Pneumonia: community-acquired

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- *Staphylococcus aureus*: commonly after the 'flu
- atypical pneumonias (e.g. Due to *Mycoplasma pneumoniae*)
- viruses

*Klebsiella pneumoniae* is classically in alcoholics

***Streptococcus pneumoniae* (pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

## Management

The British Thoracic Society published guidelines in 2009:

- low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital
- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin

Which one of the following is the main criteria for determining whether a patient with chronic obstructive pulmonary disease (COPD) should be offered long-term oxygen therapy?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Two arterial blood gases measurements with $pO_2 < 6.3$ kPa |
| <input type="radio"/> | B. One arterial blood gas measurement with $pO_2 < 7.7$ kPa    |
| <input type="radio"/> | C. One arterial blood gas measurement with $pO_2 < 8.3$ kPa    |
| <input type="radio"/> | D. One arterial blood gas measurement with $pO_2 < 8.0$ kPa    |
| <input type="radio"/> | E. Two arterial blood gases measurements with $pO_2 < 7.3$ kPa |

[Next question](#)

COPD - LTOT if 2 measurements of  $pO_2 < 7.3$  kPa

### COPD: long-term oxygen therapy

The 2010 NICE guidelines on COPD clearly define which patients should be assessed for and offered long-term oxygen therapy (LTOT). Patients who receive LTOT should breathe supplementary oxygen for at least 15 hours a day. Oxygen concentrators are used to provide a fixed supply for LTOT.

Assess patients if any of the following:

- very severe airflow obstruction ( $FEV_1 < 30\%$  predicted). Assessment should be 'considered' for patients with severe airflow obstruction ( $FEV_1 30-49\%$  predicted)
- cyanosis
- polycythaemia
- peripheral oedema
- raised jugular venous pressure
- oxygen saturations less than or equal to 92% on room air

Assessment is done by measuring arterial blood gases on 2 occasions at least 3 weeks apart in patients with stable COPD on optimal management.

Offer LTOT to patients with a  $pO_2$  of  $< 7.3$  kPa or to those with a  $pO_2$  of  $7.3 - 8$  kPa and one of the following:

- secondary polycythaemia
- nocturnal hypoxaemia
- peripheral oedema
- pulmonary hypertension

You are asked to interpret the post-bronchodilator spirometry results of a 56-year-old woman who has been complaining of progressive shortness-of-breath.

<b>FEV1/FVC</b>	0.60
<b>FEV1% predicted</b>	60%

What is the most appropriate interpretation of these results?

- ☐ A. Poor technique - repeat spirometry
- ☐ B. Asthma
- ☐ C. COPD (stage 1 - mild)
- ☐ D. COPD (stage 2 - moderate)
- ☐ E. Pulmonary fibrosis

Next question

### COPD: investigation and diagnosis

NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are smokers or ex-smokers and have symptoms such as exertional breathlessness, chronic cough or regular sputum production.

The following investigations are recommended in patients with suspected COPD:

- post-bronchodilator spirometry to demonstrate airflow obstruction: FEV1/FVC ratio less than 70%
- chest x-ray: hyperinflation, bullae, flat hemidiaphragm. Also important to exclude lung cancer
- full blood count: exclude secondary polycythaemia
- body mass index (BMI) calculation

The severity of COPD is categorised using the FEV1\*:

Post-bronchodilator FEV1/FVC	FEV1 (of predicted)	Severity
< 0.7	> 80%	Stage 1 - Mild**
< 0.7	50-79%	Stage 2 - Moderate
< 0.7	30-49%	Stage 3 - Severe
< 0.7	< 30%	Stage 4 - Very severe

Measuring peak expiratory flow is of limited value in COPD, as it may underestimate the degree of airflow obstruction.

\*note that the grading system has changed following the 2010 NICE guidelines. If the FEV1 is greater than 80% predicted but the post-bronchodilator FEV1/FVC is < 0.7 then this is classified as Stage 1 - mild

\*\*symptoms should be present to diagnose COPD in these patients

A 41-year-old man presents to his doctor with a persistent cough. This has been present for the past six months and for the past two weeks he has been coughing up blood on a daily basis. He also feels more short-of-breath when exerting himself than normal. He is a non-smoker and has no past medical history of note. On examination he is noted to have reduced air entry in the right upper zone. A chest x-ray shows a right upper lobe collapse and a subsequent bronchoscopy demonstrates a cherry-red lesion in the right superior lobar bronchus. What is the most likely diagnosis?

<input type="radio"/>	A. Small cell lung carcinoma
<input type="radio"/>	B. Large cell lung carcinoma.
<input type="radio"/>	C. Lung carcinoid
<input type="radio"/>	D. Bronchioloalveolar carcinoma
<input type="radio"/>	E. Bronchial adenocarcinoma

[Next question](#)

The 'cherry-red' lesion is a typical finding of lung carcinoid.

### Lung cancer: carcinoid

The vast majority of bronchial adenomas are carcinoid tumours, arising from the amine precursor uptake and decarboxylation (APUD) system, like small cell tumours. Lung carcinoid accounts 1% of lung tumours and for 10% of carcinoid tumours. The term bronchial adenoma is being phased out.

#### Lung carcinoid

- typical age = 40-50 years
- smoking not risk factor
- slow growing: e.g. long history of cough, recurrent haemoptysis
- often centrally located and not seen on CXR
- 'cherry red ball' often seen on bronchoscopy
- carcinoid syndrome itself is rare (associated with liver metastases)

#### Management

- surgical resection
- if no metastases then 90% survival at 5 years

You are reviewing a 40-year-old man who is known to have bronchiectasis. What organism is most likely to be isolated from his sputum?

<input type="radio"/>	A. <i>Streptococcus pneumoniae</i>
<input type="radio"/>	B. <i>Klebsiella</i> spp.
<input type="radio"/>	C. <i>Haemophilus influenzae</i>
<input type="radio"/>	D. <i>Pneumocystis jiroveci</i>
<input type="radio"/>	E. <i>Pseudomonas aeruginosa</i>

[Next question](#)

Bronchiectasis: most common organism = *Haemophilus influenzae*

### Bronchiectasis: management

Bronchiectasis describes a permanent dilatation of the airways secondary to chronic infection or inflammation. After assessing for treatable causes (e.g. immune deficiency) management is as follows:

- physical training (e.g. inspiratory muscle training) - has a good evidence base for patients with non-cystic fibrosis bronchiectasis
- postural drainage
- antibiotics for exacerbations + long-term rotating antibiotics in severe cases
- bronchodilators in selected cases
- immunisations
- surgery in selected cases (e.g. Localised disease)

Most common organisms isolated from patients with bronchiectasis:

- *Haemophilus influenzae* (most common)
- *Pseudomonas aeruginosa*
- *Klebsiella* spp.
- *Streptococcus pneumoniae*

A 37-year-old woman who is being treated as an inpatient for *Mycoplasma pneumoniae* is reviewed. Unfortunately she is unable to tolerate clarithromycin due to severe nausea. What is the most suitable alternative antibiotic?

<input type="radio"/>	A. Linezolid
<input type="radio"/>	B. Cefaclor
<input type="radio"/>	C. Ciprofloxacin
<input type="radio"/>	D. Co-amoxiclav
<input type="radio"/>	E. Doxycycline

[Next question](#)

*Mycoplasma pneumoniae* if allergic/intolerant to macrolides - doxycycline

### ***Mycoplasma pneumoniae***

*Mycoplasma pneumoniae* is a cause of atypical pneumonia which often affects younger patients. It is associated with a number of characteristic complications such as erythema multiforme and cold autoimmune haemolytic anaemia. Epidemics of *Mycoplasma pneumoniae* classically occur every 4 years. It is important to recognise atypical pneumonias as they may not respond to penicillins or cephalosporins

#### Features

- the disease typically has a prolonged and gradual onset
- flu-like symptoms classically precede a dry cough
- bilateral consolidation on x-ray
- complications may occur as below

#### Complications

- cold agglutins (IgM) may cause an haemolytic anaemia, thrombocytopenia
- erythema multiforme, erythema nodosum
- meningoencephalitis, Guillain-Barre syndrome
- bullous myringitis: painful vesicles on the tympanic membrane
- pericarditis/myocarditis
- gastrointestinal: hepatitis, pancreatitis
- renal: acute glomerulonephritis

#### Diagnosis

- *Mycoplasma* serology

## Management

- erythromycin/clarithromycin
- tetracyclines such as doxycycline are an alternative



A 60-year-old female with a history of COPD presents to the Emergency Department with shortness of breath. Blood pressure is 120/80 mmHg and her pulse is 90 bpm. The chest x-ray shows a pneumothorax with a 2.5 cm rim of air and no mediastinal shift. What is the most appropriate management?

<input type="radio"/>	A. Intercostal drain insertion
<input type="radio"/>	B. Discharge
<input type="radio"/>	C. Admit for 48 hours observation and repeat chest x-ray
<input type="radio"/>	D. Immediate 14G cannula into 2nd intercostal space, mid-clavicular line
<input type="radio"/>	E. Aspiration

[Next question](#)

## Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

### Primary pneumothorax

Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails (defined as > 2 cm or still short of breath) then a chest drain should be inserted

### Secondary pneumothorax

Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and/or the patient is short of breath then a chest drain should be inserted.
- otherwise aspiration should be attempted if the rim of air is between 1-2cm. If aspiration fails (i.e. pneumothorax is still greater than 1cm) a chest drain should be inserted. All patients should be admitted for at least 24 hours
- if the pneumothorax is less than 1cm then the BTS guidelines suggest giving oxygen and admitting for 24 hours
- regarding scuba diving, the BTS guidelines state: *'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'*

## **Iatrogenic pneumothorax**

Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD

A 27-year-old man with no significant past medical history of note presents to the Emergency Department with a one day history of dyspnoea and right-sided pleuritic chest pain. A chest x-ray is taken which shows a right pneumothorax with a 2.5cm rim of air and no mediastinal shift. Aspiration is performed by the admitting doctor.

He is reviewed four hours later. His dyspnoea has resolved but the chest x-ray shows that whilst the pneumothorax has improved there is still a 1.5cm rim of air. What is the most appropriate management?

<input type="radio"/>	A. Repeat aspiration
<input type="radio"/>	B. Intercostal drain insertion
<input type="radio"/>	C. Refer to a cardiothoracic surgeon for pleurodesis
<input type="radio"/>	D. Admit for observation
<input type="radio"/>	E. Discharge with outpatient chest x-ray

[Next question](#)

The British Thoracic Society algorithm for spontaneous pneumothorax suggests that if following aspiration the rim of air is < 2cm and the breathing has improved then discharge should be considered with outpatient review.

## Pneumothorax

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### Primary pneumothorax

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Recommendations include:

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- ventilated patients need chest drains, as may some patients with COPD

A 30-year-old woman is admitted to the Emergency Department with an exacerbation of asthma. On arrival her peak flow is 30% of predicted, respiratory rate is 36/min and oxygen saturations are 98% on 100% high-flow oxygen. She is given back-to-back nebulisers, intravenous hydrocortisone and started on a magnesium infusion. Which one of the following would be the strongest indicator of a need for intubation and ventilation?

- ☐ A. PEFR 20% of predicted
- ☐ B. pH 7.33
- ☐ C. Patient preference after informed consent
- ☐ D. Respiratory rate of 50 / min
- ☐ E. Oxygen saturations of 95% on 100% high-flow oxygen

Next question

A falling pH likely represents carbon dioxide retention in a tiring patient as is an ominous sign in acute asthma. Performing serial peak flows in a patient with life-threatening asthma is neither practical nor desirable.

### Asthma: acute severe

Patients with acute severe asthma are stratified into moderate, severe or life-threatening

Moderate	Severe	Life-threatening
<ul style="list-style-type: none"> <li>• PEF &gt; 50% best or predicted</li> <li>• Speech normal</li> <li>• RR &lt; 25 / min</li> <li>• Pulse &lt; 110 bpm</li> </ul>	<ul style="list-style-type: none"> <li>• PEF 33 - 50% best or predicted</li> <li>• Can't complete sentences</li> <li>• RR &gt; 25/min</li> <li>• Pulse &gt; 110 bpm</li> </ul>	<ul style="list-style-type: none"> <li>• PEF &lt; 33% best or predicted</li> <li>• Oxygen sats &lt; 92%</li> <li>• Silent chest, cyanosis or feeble respiratory effort</li> <li>• Bradycardia, dysrhythmia or hypotension</li> <li>• Exhaustion, confusion or coma</li> </ul>

### British Thoracic Society guidelines

- magnesium sulphate recommended as next step for patients who are not responding (e.g. 1.2 - 2g IV over 20 mins)
- little evidence to support use of IV aminophylline (although still mentioned in management plans)
- if no response consider IV salbutamol

You are reviewing a man with haemoptysis in the rapid-access lung clinic. Which one of the following is the most significant risk factor for developing lung cancer?

<input type="radio"/>	A. Cryptogenic fibrosing alveolitis
<input type="radio"/>	B. Asbestos exposure for most of working life
<input type="radio"/>	C. 10 year period of smoking 'crack' cocaine 20 years ago
<input type="radio"/>	D. 30 pack-year history of smoking
<input type="radio"/>	E. 20 year history of recreational cannabis use

[Next question](#)

### Lung cancer: risk factors

#### Smoking

- increases risk of lung ca by a factor of 10

#### Other factors

- asbestos - increases risk of lung ca by a factor of 5
- arsenic
- radon
- nickel
- chromate
- aromatic hydrocarbon
- cryptogenic fibrosing alveolitis

#### Factors that are NOT related

- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a  $10 * 5 = 50$  times increased risk

A 72-year-old man presents with gradually increasing shortness-of-breath on exertion over the past six months. He stopped smoking around 20 years ago and had a number of jobs including a builder and miner when he was younger. On auscultation of his chest fine crackles can be heard in both bases. Oxygen saturations are 95% on room air.

A number of tests are arranged:

- spirometry: normal
- chest x-ray: diffuse reticular shadowing suggestive of fibrosis affecting the lower zones. Heart size normal.

What is the most likely diagnosis?

<input type="radio"/>	A. Extrinsic allergic alveolitis
<input type="radio"/>	B. Histiocytosis
<input type="radio"/>	C. Asbestosis
<input type="radio"/>	D. Silicosis
<input type="radio"/>	E. Coal worker's pneumoconiosis

Next question

Asbestosis is the only one of the above diagnoses that predominately affects the lower zones. Cryptogenic fibrosing alveolitis is of course a differential diagnosis in this scenario.

### Lung fibrosis

It is important in the exam to be able to differentiate between conditions causing predominately upper or lower zone fibrosis. It should be noted that the more common causes (cryptogenic fibrosing alveolitis, drugs) tend to affect the lower zones

Fibrosis predominately affecting the upper zones

- extrinsic allergic alveolitis
- coal worker's pneumoconiosis/progressive massive fibrosis
- silicosis
- sarcoidosis
- ankylosing spondylitis (rare)
- histiocytosis
- tuberculosis

Fibrosis predominately affecting the lower zones

- cryptogenic fibrosing alveolitis
- most connective tissue disorders (except ankylosing spondylitis)
- drug-induced: amiodarone, bleomycin, methotrexate
- asbestosis



A 34-year-old steelworker presents complaining of episodic shortness of breath. This is particularly noted whilst at work where he describes feeling wheezy and having a tendency to cough. Which one of the following is the most appropriate diagnostic investigation?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Patch testing                                     |
| <input type="radio"/> | B. High resolution computed tomography of thorax     |
| <input type="radio"/> | C. Serial peak flow measurements at work and at home |
| <input type="radio"/> | D. Specific IgE measurements                         |
| <input type="radio"/> | E. Skin prick test                                   |

[Next question](#)

Serial peak flow measurements at work and at home are used to detect occupational asthma

## Asthma: occupational

### Causes

- isocyanates - the most common cause. Example occupations include spray painting and foam moulding using adhesives
- platinum salts
- soldering flux resin
- glutaraldehyde
- flour
- epoxy resins
- proteolytic enzymes

### Diagnosis

- specific recommendations are made in the 2007 joint British Thoracic Society and SIGN guidelines
- serial measurements of peak expiratory flow are recommended at work and away from work

A 35-year-old patient with a history of asthma and epilepsy presents with haemoptysis and a worsening of his asthma. Blood tests reveal an eosinophilia and a positive pANCA. Which of the following drugs is most likely to have precipitated the likely diagnosis?

<input type="radio"/>	A. Montelukast
<input type="radio"/>	B. Phenytoin
<input type="radio"/>	C. Sodium valproate
<input type="radio"/>	D. Prednisolone
<input type="radio"/>	E. Sodium cromoglycate

[Next question](#)

This patient probably has Churg-Strauss syndrome, which is associated with the use of leukotriene receptor antagonists

### Churg-Strauss syndrome

Churg-Strauss syndrome is an ANCA associated small-medium vessel vasculitis

#### Features

- asthma
- blood eosinophilia (e.g. > 10%)
- paranasal sinusitis
- mononeuritis multiplex
- pANCA positive in 60%

Leukotriene receptor antagonists may precipitate the disease

A 63-year-old man is noted to have a pleural effusion on CXR. Which one of the following would typically cause a transudate?

<input type="radio"/>	A. Pancreatitis
<input type="radio"/>	B. Pneumonia
<input type="radio"/>	C. Yellow nail syndrome
<input type="radio"/>	D. Hypothyroidism
<input type="radio"/>	E. Dressler's syndrome

[Next question](#)

### Pleural effusion

Exudate (> 30g/L protein)

- infection: pneumonia, TB, subphrenic abscess
- connective tissue disease: RA, SLE
- neoplasia: lung cancer, mesothelioma, metastases
- pancreatitis
- pulmonary embolism
- Dressler's syndrome
- yellow nail syndrome

Transudate (< 30g/L protein)

- heart failure
- hypoalbuminaemia (liver disease, nephrotic syndrome, malabsorption)
- hypothyroidism
- Meigs' syndrome

You are reviewing a patient with chronic obstructive pulmonary disease (COPD) who remains breathless despite using a salbutamol inhaler as required. Their FEV1 is 60%. What are the two main options?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | <b>A.</b> Long-acting beta2-agonist (LABA) <b>or</b> inhaled corticosteroid   |
| <input type="radio"/> | <b>B.</b> Long-acting muscarinic antagonist (LAMA) + inhaled corticosteroid (ICS) in a combination inhaler <b>or</b> long-acting beta2-agonist (LABA) |
| <input type="radio"/> | <b>C.</b> Long-acting beta2-agonist (LABA) <b>or</b> LABA + inhaled corticosteroid (ICS) in a combination inhaler                                     |
| <input type="radio"/> | <b>D.</b> Long-acting beta2-agonist (LABA) <b>or</b> regular combined short-acting beta2-agonist + muscarinic antagonist (e.g. Combivent)             |
| <input type="radio"/> | <b>E.</b> Long-acting beta2-agonist (LABA) <b>or</b> long-acting muscarinic antagonist (LAMA)   |

Next question

COPD - still breathless despite using inhalers as required?

- FEV1 > 50%: LABA **or** LAMA
- FEV1 < 50%: LABA + ICS **or** LAMA

### COPD: stable management

NICE updated its guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

#### General management

- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

#### Bronchodilator therapy

- a short-acting beta2-agonist (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%

- long-acting beta2-agonist (LABA), for example salmeterol, or:

- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%

- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness

- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline

- NICE only recommends theophylline after trials of short and long-acting bronchodilators or to people who cannot use inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics

- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale

- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD

- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

A 62-year-old woman with recently diagnosed chronic obstructive pulmonary disease (COPD) presents for review. Her FEV1 is 65% of the predicted value. She has managed to give up smoking and was prescribed a salbutamol inhaler to use as required. Despite this she is still symptomatic and complains of wheeze and shortness of breath. What is the most appropriate next step?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Add an inhaled corticosteroid  |
| <input type="radio"/> | B. Add a long-acting muscarinic antagonist inhaler                        |
| <input type="radio"/> | C. Refer for consideration of long-term oxygen therapy                    |
| <input type="radio"/> | D. Add oral theophylline  |
| <input type="radio"/> | E. Add a combination long-acting beta2-agonist and corticosteroid inhaler |

[Next question](#)

Following the 2010 NICE guidelines a long-acting beta2-agonist (LABA) would be an alternative option.

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#### FEV1 > 50%

- long-acting beta2-agonist (LABA), for example salmeterol, or:
- long-acting muscarinic antagonist (LAMA), for example tiotropium

#### FEV1 < 50%

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- LAMA

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**Question 114 of 134**

Next

A 65-year-old life-long smoker with a significant past history of asbestos exposure is investigated for lung cancer. Given his history of both smoking and asbestos exposure, what is his increased risk of lung cancer?

<input type="radio"/>	A. 5
<input type="radio"/>	B. 10
<input type="radio"/>	C. 50
<input type="radio"/>	D. 500
<input type="radio"/>	E. 1,000

Next question

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a  $10 * 5 = 50$  times increased risk

**Lung cancer: risk factors**

## Smoking

- increases risk of lung ca by a factor of 10

## Other factors

- asbestos - increases risk of lung ca by a factor of 5
- arsenic
- radon
- nickel
- chromate
- aromatic hydrocarbon
- cryptogenic fibrosing alveolitis

## Factors that are NOT related

- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a  $10 * 5 = 50$  times increased risk



A 17-year-old male with a history of cystic fibrosis presents to clinic for annual review. What is the most appropriate advice regarding his diet?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. High calorie and low fat with pancreatic enzyme supplementation for every meal    |
| <input type="radio"/> | B. High calorie and low fat with pancreatic enzyme supplementation for evening meal  |
| <input type="radio"/> | C. Normal calorie and low fat with pancreatic enzyme supplementation for every meal  |
| <input type="radio"/> | D. High calorie and high fat with pancreatic enzyme supplementation for evening meal |
| <input type="radio"/> | E. High calorie and high fat with pancreatic enzyme supplementation for every meal   |

[Next question](#)

Please see the link for more details.

### Cystic fibrosis: management

Management of cystic fibrosis involves a multidisciplinary approach

#### Key points

- regular (at least twice daily) chest physiotherapy and postural drainage. Parents are usually taught to do this. Deep breathing exercises are also useful
- high calorie diet, including high fat intake\*
- vitamin supplementation
- pancreatic enzyme supplements taken with meals
- heart and lung transplant

\*this is now the standard recommendation - previously high calorie, low-fat diets have been recommended to reduce the amount of steatorrhoea

A chest x-ray of a patient with sarcoidosis shows bilateral hilar lymphadenopathy accompanied with interstitial infiltrates. What chest x-ray stage does this correspond to?

<input type="radio"/>	A. Stage 0
<input type="radio"/>	B. Stage 1
<input type="radio"/>	C. Stage 2
<input type="radio"/>	D. Stage 3
<input type="radio"/>	E. Stage 4

[Next question](#)

#### Sarcoidosis CXR

- 1 = BHL
- 2 = BHL + infiltrates
- 3 = infiltrates
- 4 = fibrosis

#### Sarcoidosis: investigation

There is no one diagnostic test for sarcoidosis and hence diagnosis is still largely clinical. ACE levels have a sensitivity of 60% and specificity of 70% and are therefore not reliable in the diagnosis of sarcoidosis although they may have a role in monitoring disease activity. Routine bloods may show hypercalcaemia (seen in 10% of patients) and a raised ESR

A chest x-ray may show the following changes:

- stage 0 = normal
- stage 1 = bilateral hilar lymphadenopathy (BHL)
- stage 2 = BHL + interstitial infiltrates
- stage 3 = diffuse interstitial infiltrates only
- stage 4 = diffuse fibrosis

Other investigations\*

- spirometry: may show a restrictive defect
- tissue biopsy: non-caseating granulomas
- gallium-67 scan - not used routinely

\*the Kveim test (where part of the spleen from a patient with known sarcoidosis is injected under the skin) is no longer performed due to concerns about cross-infection

**Question 117 of 134**

Next

A 66-year-old man with a history of chronic obstructive pulmonary disease (COPD) is referred by his GP to the Rapid Access Chest Clinic. He was recently treated with several courses of antibiotics and steroids for an exacerbation of COPD which failed to completely resolve. A chest x-ray was reported as follows:

There is a suspicious 3cm mass in the right hilum. Background changes of COPD. Urgent referral to the chest clinic is advised.

\*\*\*Report faxed to GP\*\*\*

Recent blood tests are also reviewed:

Hb	14.2 g/dl
Platelets	$323 \times 10^9/l$
WBC	$9.1 \times 10^9/l$

Na <sup>+</sup>	128 mmol/l
K <sup>+</sup>	3.9 mmol/l
Urea	6.4 mmol/l
Creatinine	99 $\mu$ mol/l

On examination there is no evidence of clubbing. Examination of chest demonstrates a fixed monophonic wheeze in the right lung. What is the most likely underlying cause?

- ☐ A. Tuberculosis
- ☐ B. Sarcoidosis
- ☐ C. Squamous cell lung cancer
- ☒ D. Small cell lung cancer
- ☐ E. Lymphoma

Next question

The presence of hyponatraemia strongly points towards a diagnosis of small cell lung cancer.

**Lung cancer: small cell****Features**

- usually central
- arise from APUD\* cells
- associated with ectopic ADH, ACTH secretion
- ADH --> hyponatraemia
- ACTH --> Cushing's syndrome

- ACTH secretion can cause bilateral adrenal hyperplasia, the high levels of cortisol can lead to hypokalaemic alkalosis
- Lambert-Eaton syndrome: antibodies to voltage gated calcium channels causing myasthenic like syndrome

## Management

- usually metastatic disease by time of diagnosis
- surgery: only used for debulking
- most patients with limited disease now receive a combination of chemotherapy and radiotherapy
- patients with more extensive disease are offered palliative chemotherapy

\*an acronym for

- Amine - high amine content
- Precursor Uptake - high uptake of amine precursors
- Decarboxylase - high content of the enzyme decarboxylase

A 49-year-old female is admitted to the Emergency Department with shortness of breath. On examination the pulse is 114 bpm with blood pressure 106/66 mmHg, temperature 37.7°C and respiratory rate 30/min. Examination of the cardiorespiratory system is unremarkable with a peak expiratory flow rate of 400 l/min. Arterial blood gases on air reveal:

pH	7.41
pCO <sub>2</sub>	4.0 kPa
pO <sub>2</sub>	7.2 kPa

Following the initiation of oxygen therapy, what is the next most important step in management?

- ☐ A. IV aminophylline
- ☐ B. IV hydrocortisone
- ☐ C. Low molecular weight heparin
- ☐ D. IV fluids
- ☐ E. IV co-trimoxazole

Next question

Type 1 respiratory failure in a tachycardic, tachypnoeic female with an absence of chest signs points towards a diagnosis of pulmonary embolism.

Low-grade pyrexia is common in pulmonary embolism.

### Pulmonary embolism: management

The NICE guidelines of 2012 provided some clarity on how long patients should be anticoagulated for after a pulmonary embolism (PE). Selected points are listed below.

Low molecular weight heparin (LMWH) or fondaparinux should be given initially after a PE is diagnosed. An exception to this is for patients with a massive PE where thrombolysis is being considered. In such a situation unfractionated heparin should be used.

- a vitamin K antagonist (i.e. warfarin) should be given within 24 hours of the diagnosis
- the LMWH or fondaparinux should be continued for at least 5 days or until the international normalised ratio (INR) is 2.0 or above for at least 24 hours, whichever is longer, i.e. LMWH or fondaparinux is given at the same time as warfarin until the INR is in the therapeutic range
- warfarin should be continued for at least 3 months. At 3 months, NICE advise that clinicians should 'assess the risks and benefits of extending treatment'
- NICE advise extending warfarin beyond 3 months for patients with *unprovoked* PE. This essentially means that if there was no obvious cause or provoking factor (surgery, trauma, significant immobility) it may imply the patient has a tendency to thrombosis and should be given treatment longer than the norm of 3 months

- for patients with active cancer NICE recommend using LMWH for 6 months

## Thrombolysis

- thrombolysis is now recommended as the first-line treatment for massive PE where there is circulatory failure (e.g. hypotension). Other invasive approaches should be considered where appropriate facilities exist

**Question 119 of 134**

Next

A middle-aged woman is admitted to the Emergency Department with pleuritic chest pain ten days after having a hysterectomy. There is a clinical suspicion of pulmonary embolism. What is the most common chest x-ray finding in patients with pulmonary embolism?

- ☐ A. Right heart enlargement
- ☐ B. Normal
- ☐ C. Pleural effusion
- ☐ D. Linear atelectasis
- ☐ E. Dilatation of the pulmonary vessels proximal to the embolism

Next question

Pulmonary embolism - normal CXR

The vast majority of patients with a pulmonary embolism have a normal chest x-ray.

**Pulmonary embolism: investigation****2012 NICE guidelines**

All patients with symptoms or signs suggestive of a PE should have a history taken, examination performed and a chest x-ray to exclude other pathology.

If a PE is still suspected a two-level PE Wells score should be performed:

Clinical feature	Points
Clinical signs and symptoms of DVT (minimum of leg swelling and pain with palpation of the deep veins)	3
An alternative diagnosis is less likely than PE	3
Heart rate > 100 beats per minute	1.5
Immobilisation for more than 3 days or surgery in the previous 4 weeks	1.5
Previous DVT/PE	1.5
Haemoptysis	1
Malignancy (on treatment, treated in the last 6 months, or palliative)	1

Clinical probability simplified scores

- PE likely - more than 4 points
- PE unlikely - 4 points or less

If a PE is 'likely' (more than 4 points) arrange an immediate computed tomography pulmonary angiogram (CTPA). If there is a delay in getting the CTPA then give low-molecular weight heparin until the scan is performed.

If a PE is 'unlikely' (4 points or less) arranged a D-dimer test. If this is positive arrange an immediate computed tomography pulmonary angiogram (CTPA). If there is a delay in getting the CTPA then give low-molecular weight heparin until the scan is performed.

If the patient has an allergy to contrast media or renal impairment a V/Q scan should be used instead of a CTPA.

### **CTPA or V/Q scan?**

The British Thoracic Society (BTS) published guidelines back in 2003 on the management of patients with suspected pulmonary embolism (PE). Key points from the guidelines include:

- computed tomographic pulmonary angiography (CTPA) is now the recommended initial lung-imaging modality for non-massive PE. Advantages compared to V/Q scans include speed, easier to perform out-of-hours, a reduced need for further imaging and the possibility of providing an alternative diagnosis if PE is excluded
- if the CTPA is negative then patients do not need further investigations or treatment for PE
- ventilation-perfusion scanning may be used initially if appropriate facilities exist, the chest x-ray is normal, and there is no significant symptomatic concurrent cardiopulmonary disease

### **Some other points**

#### **D-dimers**

- sensitivity = 95-98%, but poor specificity

#### **ECG**

- the classic ECG changes seen in PE are a large S wave in lead I, a large Q wave in lead III and an inverted T wave in lead III - 'S1Q3T3'. However this change is seen in no more than 20% of patients
- right bundle branch block and right axis deviation are also associated with PE
- sinus tachycardia may also be seen

#### **V/Q scan**

- sensitivity = 98%; specificity = 40% - high negative predictive value, i.e. if normal virtually excludes PE
- other causes of mismatch in V/Q include old pulmonary embolisms, AV malformations, vasculitis, previous radiotherapy
- COPD gives matched defects

#### **CTPA**



- peripheral emboli affecting subsegmental arteries may be missed

#### Pulmonary angiography

- the gold standard
- significant complication rate compared to other investigations

**Question 120 of 134**

Next

A 25-year-old man is referred due to pain and swelling in his knees and ankles. On examination he has a painful, erythematous rash on his legs. The following results are obtained:

Rheumatoid factor	Negative
ESR	94 mm/hr
Chest x-ray	Hilar lymphadenopathy

What is the most likely outcome?

- ☐ A. Improvement following a course of prednisolone
- ☐ B. Scarring and ulceration of skin
- ☐ C. Spontaneous improvement
- ☐ D. Progressive arthritis
- ☐ E. Renal replacement therapy in 20 years time

Next question

The majority of patients with sarcoidosis get better without treatment

This man has an acute form of sarcoidosis. There are no indications for steroid therapy and his symptoms will resolve spontaneously in the majority of cases

**Sarcoidosis: prognostic features**

Sarcoidosis is a multisystem disorder of unknown aetiology characterised by non-caseating granulomas. It is more common in young adults and in people of African descent. Sarcoidosis remits without treatment in approximately two-thirds of people

Factors associated with poor prognosis

- insidious onset, symptoms > 6 months
- absence of erythema nodosum
- extrapulmonary manifestations: e.g. lupus pernio, splenomegaly
- CXR: stage III-IV features
- black people

**Question 121 of 134**

Next

A 35-year-old female presents with shortness of breath. The following blood gases are obtained on room air:

pH	7.54
pCO <sub>2</sub>	1.8 kPa
pO <sub>2</sub>	12.4 kPa

Which one of the following is the least likely cause?

<input type="radio"/>	A. Opiate overdose
<input type="radio"/>	B. Pulmonary embolism
<input type="radio"/>	C. Pregnancy
<input type="radio"/>	D. Encephalitis
<input type="radio"/>	E. Anxiety

Next question

The question asks for the least likely cause of a respiratory alkalosis. Salicylate, not opiate, poisoning is associated with a respiratory alkalosis. Opiate overdose would lead to respiratory depression and hence a respiratory acidosis

**Respiratory alkalosis**

Common causes

- anxiety leading to hyperventilation
- pulmonary embolism
- salicylate poisoning\*
- CNS disorders: stroke, subarachnoid haemorrhage, encephalitis
- altitude
- pregnancy

\*salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis

A 74-year-old woman has a chest x-ray organised by her GP due to a chronic cough. The chest x-ray shows a cavity in the left upper zone inside of which there is a solid mass. An aspergilloma is suspected. What is the most appropriate next test?

<input type="radio"/>	A. Sputum culture
<input type="radio"/>	B. Serology for Aspergillus precipitins
<input type="radio"/>	C. Blood culture
<input type="radio"/>	D. Bronchoscopy with biopsy
<input type="radio"/>	E. Transthoracic fine needle biopsy

[Next question](#)

## Aspergilloma

An aspergilloma is a fungus ball which often colonises an existing lung cavity (e.g. secondary to TB, lung cancer or cystic fibrosis)

Usually asymptomatic but features may include

- cough
- haemoptysis (may be severe)

Investigations

- CXR containing a rounded opacity
- high titres Aspergillus precipitins

A 24-year-old man who has been discharged following admission for a spontaneous pneumothorax ask for advice about flying. During his stay in hospital the pneumothorax was aspirated and a check x-ray revealed no residual air. What is the earliest time he should fly?

<input type="radio"/>	A. Immediately
<input type="radio"/>	B. 24 hours
<input type="radio"/>	C. 3 days
<input type="radio"/>	D. 2 weeks
<input type="radio"/>	E. 2 months

[Next question](#)

Please see the text below for an explanation about the competing and changing guidelines.

### Fitness to fly

The Civil Aviation Authority (CAA) has issued guidelines on air travel for people with medical conditions; please see the link provided.

#### Cardiovascular disease

- unstable angina, uncontrolled hypertension, uncontrolled cardiac arrhythmia, decompensated heart failure, severe symptomatic valvular disease: should not fly
- uncomplicated myocardial infarction: may fly after 7-10 days
- complicated myocardial infarction: after 4-6 weeks
- coronary artery bypass graft: after 10-14 days
- percutaneous coronary intervention: after 5 days

#### Respiratory disease

- pneumonia: should be 'clinically improved with no residual infection'
- pneumothorax: absolute contraindication, the CAA suggest patients may travel 2 weeks after successful drainage if there is no residual air. The British Thoracic Society used to recommend not travelling by air for a period of 6 weeks but this has now been changed to 1 week post check x-ray

#### Pregnancy

- most airlines do not allow travel after 36 weeks for a single pregnancy and after 32 weeks for a multiple pregnancy
- most airlines require a certificate after 28 weeks confirming that the pregnancy is progressing normally

## Surgery

- travel should be avoided for 10 days following abdominal surgery
- laparoscopic surgery: after 24 hours
- colonoscopy: after 24 hours
- following the application of a plaster cast, the majority of airlines restrict flying for 24 hours on flights of less than 2 hours or 48 hours for longer flights

## Haematological disorders

- patients with a haemoglobin of greater than 8 g/dl may travel without problems (assuming there is no coexisting condition such as cardiovascular or respiratory disease)

When assessing a patient with suspected chronic obstructive pulmonary disease, which one of the following is least relevant?

<input type="radio"/>	A. Smoking history
<input type="radio"/>	B. Chest x-ray
<input type="radio"/>	C. Full blood count
<input type="radio"/>	D. Peak expiratory flow
<input type="radio"/>	E. Spirometry

[Next question](#)

Peak expiratory flow is of no value in the diagnosis of COPD

### COPD: investigation and diagnosis

NICE recommend considering a diagnosis of COPD in patients over 35 years of age who are smokers or ex-smokers and have symptoms such as exertional breathlessness, chronic cough or regular sputum production.

The following investigations are recommended in patients with suspected COPD:

- post-bronchodilator spirometry to demonstrate airflow obstruction: FEV1/FVC ratio less than 70%
- chest x-ray: hyperinflation, bullae, flat hemidiaphragm. Also important to exclude lung cancer
- full blood count: exclude secondary polycythaemia
- body mass index (BMI) calculation

The severity of COPD is categorised using the FEV1\*:

Post-bronchodilator FEV1/FVC	FEV1 (of predicted)	Severity
< 0.7	> 80%	Stage 1 - Mild**
< 0.7	50-79%	Stage 2 - Moderate
< 0.7	30-49%	Stage 3 - Severe
< 0.7	< 30%	Stage 4 - Very severe

Measuring peak expiratory flow is of limited value in COPD, as it may underestimate the degree of airflow obstruction.

\*note that the grading system has changed following the 2010 NICE guidelines. If the FEV1 is greater than 80% predicted but the post-bronchodilator FEV1/FVC is < 0.7 then this is classified as Stage 1 - mild

\*\*symptoms should be present to diagnose COPD in these patients

A 19-year-old with 'brittle asthma' is seen in clinic. Three weeks ago she started taking prednisolone 15mg od as her asthma was poorly controlled on beclometasone dipropionate 800 mcg bd., salmeterol, oral montelukast and salbutamol as required. What should happen with regards to inhaled steroids?

- ☐ A. Continue beclometasone dipropionate 800 mcg bd
- ☐ B. Stop inhaled steroids
- ☐ C. Increase beclometasone dipropionate to 1000 mcg bd
- ☐ D. Decrease beclometasone dipropionate to 400 mcg bd
- ☐ E. Use beclometasone dipropionate 200 mcg on an 'as required' basis with salbutamol

Next question

Even when patients are on oral prednisolone they should continue high-dose inhaled corticosteroids

### Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

<b>Step 1</b>	Inhaled short-acting B2 agonist as required
<b>Step 2</b>	Add inhaled steroid at 200-800 mcg/day*  400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
<b>Step 3</b>	1. Add inhaled long-acting B2 agonist (LABA)  2. Assess control of asthma: <ul style="list-style-type: none"> <li>• good response to LABA - continue LABA</li> <li>• benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose)</li> <li>• no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline</li> </ul>
<b>Step 4</b>	Consider trials of: <ul style="list-style-type: none"> <li>• increasing inhaled steroid up to 2000 mcg/day*</li> <li>• addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet</li> </ul>
<b>Step 5</b>	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets  Maintain high dose inhaled steroid at 2000 mcg/day*  Refer patient for specialist care

\*beclometasone dipropionate or equivalent



## Additional notes

### Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone

Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles

Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

You are reviewing a patient with chronic obstructive pulmonary disease (COPD) who remains breathless despite using an ipratropium bromide inhaler as required. Her FEV1 is 40%. What are the two main options?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | <b>A.</b> Long-acting beta2-agonist (LABA) <b>or</b> inhaled corticosteroid   |
| <input type="radio"/> | <b>B.</b> Long-acting muscarinic antagonist (LAMA) <b>or</b> LABA + inhaled corticosteroid (ICS) in a combination inhaler                             |
| <input type="radio"/> | <b>C.</b> Long-acting beta2-agonist (LABA) <b>or</b> long-acting muscarinic antagonist (LAMA)   |
| <input type="radio"/> | <b>D.</b> Long-acting beta2-agonist (LABA) <b>or</b> regular combined short-acting beta2-agonist + muscarinic antagonist (e.g. Combivent)             |
| <input type="radio"/> | <b>E.</b> Long-acting muscarinic antagonist (LAMA) + inhaled corticosteroid (ICS) in a combination inhaler <b>or</b> long-acting beta2-agonist (LABA) |

Next question

COPD - still breathless despite using inhalers as required?

- FEV1 > 50%: LABA **or** LAMA
- FEV1 < 50%: LABA + ICS **or** LAMA

### COPD: stable management

NICE updated its guidelines on the management of chronic obstructive pulmonary disease (COPD) in 2010.

#### General management

- smoking cessation advice
- annual influenza vaccination
- one-off pneumococcal vaccination

#### Bronchodilator therapy

- a short-acting beta2-agonist (SABA) or short-acting muscarinic antagonist (SAMA) is first-line treatment
- for patients who remain breathless or have exacerbations despite using short-acting bronchodilators the next step is determined by the FEV1

FEV1 > 50%

- long-acting beta2-agonist (LABA), for example salmeterol, or:

- long-acting muscarinic antagonist (LAMA), for example tiotropium

FEV1 < 50%

- LABA + inhaled corticosteroid (ICS) in a combination inhaler, or:
- LAMA

For patients with persistent exacerbations or breathlessness

- if taking a LABA then switch to a LABA + ICS combination inhaler
- otherwise give a LAMA and a LABA + ICS combination inhaler

Oral theophylline

- NICE only recommends theophylline after trials of short and long-acting bronchodilators or to people who cannot use inhaled therapy
- the dose should be reduced if macrolide or fluoroquinolone antibiotics are co-prescribed

Mucolytics

- should be 'considered' in patients with a chronic productive cough and continued if symptoms improve

Cor pulmonale

- features include peripheral oedema, raised jugular venous pressure, systolic parasternal heave, loud P2
- use a loop diuretic for oedema, consider long-term oxygen therapy
- ACE-inhibitors, calcium channel blockers and alpha blockers are not recommended by NICE

Factors which may improve survival in patients with stable COPD

- smoking cessation - the single most important intervention in patients who are still smoking
- long term oxygen therapy in patients who fit criteria
- lung volume reduction surgery in selected patients

Non-invasive ventilation (NIV) is least likely to be successful in which one of the following scenarios?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. COPD                             |
| <input type="radio"/> | B. Chest wall deformity             |
| <input type="radio"/> | C. Obstructive sleep apnoea         |
| <input type="radio"/> | D. Weaning from tracheal intubation |
| <input type="radio"/> | E. Bronchiectasis                   |

Next question

The British Thoracic Society recommend that whilst a trial of NIV may be undertaken in bronchiectasis it should not be used routinely as its effectiveness is likely to be limited by excessive secretions

### Non-invasive ventilation

The British Thoracic Society (BTS) published guidelines in 2002 on the use of non-invasive ventilation in acute respiratory failure. Following these the Royal College of Physicians published guidelines in 2008.

Non-invasive ventilation - key indications

- COPD with respiratory acidosis pH 7.25-7.35
- type II respiratory failure secondary to chest wall deformity, neuromuscular disease or obstructive sleep apnoea
- cardiogenic pulmonary oedema unresponsive to CPAP
- weaning from tracheal intubation

Recommended initial settings for bi-level pressure support in COPD

- Expiratory Positive Airway Pressure (EPAP): 4-5 cm H<sub>2</sub>O
- Inspiratory Positive Airway Pressure (IPAP): RCP advocate 10 cm H<sub>2</sub>O whilst BTS suggest 12-15 cm H<sub>2</sub>O
- back up rate: 15 breaths/min
- back up inspiration:expiration ratio: 1:3

A 24-year-old man who has developed a chronic cough and wheeze after starting a new job presents for review. His peak flow measurements are significantly reduced whilst at work and improve at the weekend. Which one of the following substances is most frequently associated with this kind of asthma?

<input type="radio"/>	A. Cadmium
<input type="radio"/>	B. Cement dust
<input type="radio"/>	C. Diesel fumes
<input type="radio"/>	D. Isocyanates
<input type="radio"/>	E. Organophosphates (insecticides)

[Next question](#)

Isocyanates are the most common cause of occupational asthma

## Asthma: occupational

### Causes

- isocyanates - the most common cause. Example occupations include spray painting and foam moulding using adhesives
- platinum salts
- soldering flux resin
- glutaraldehyde
- flour
- epoxy resins
- proteolytic enzymes

### Diagnosis

- specific recommendations are made in the 2007 joint British Thoracic Society and SIGN guidelines
- serial measurements of peak expiratory flow are recommended at work and away from work

A 27-year-old man with a history of 'brittle' asthma is admitted to the Emergency Department with an asthma attack. The paramedics have already administered high-flow oxygen and nebulised salbutamol. He is unable to complete sentences, has a tight bilateral expiratory wheeze and is unable to perform a peak flow reading. His respiratory rate is 30 / minute, sats 94% (on high-flow oxygen) and pulse 120 / minute. He is immediately given intravenous hydrocortisone and nebulised salbutamol is given continuously. After five minutes there is no improvement and intravenous magnesium sulphate is given. After another five minutes an arterial blood gas sample is taken:

pH	7.34
pCO <sub>2</sub>	6.9 kPa
pO <sub>2</sub>	8.8 kPa

What is the most appropriate management?

<input type="radio"/>	A. Non-invasive ventilation
<input type="radio"/>	B. Add intravenous aminophylline
<input type="radio"/>	C. Give a further bolus of intravenous hydrocortisone
<input type="radio"/>	D. Add nebulised ipratropium bromide and review in 10 minutes
<input type="radio"/>	E. Intubation

This question is about clinical judgement. A review of the British Thoracic Society guidelines will show that in such a scenario nebulised ipratropium bromide should have been given much earlier but this did not happen. The above arterial blood gas results for a young asthmatic patient are alarming and suggest that he is rapidly becoming tired. It is therefore inappropriate to wait a further 10 minutes. This patient's needs ITU input with probable intubation and ventilation.

### Asthma: acute severe

Patients with acute severe asthma are stratified into moderate, severe or life-threatening

Moderate	Severe	Life-threatening
<ul style="list-style-type: none"> <li>• PEF &gt; 50% best or predicted</li> <li>• Speech normal</li> <li>• RR &lt; 25 / min</li> <li>• Pulse &lt; 110 bpm</li> </ul>	<ul style="list-style-type: none"> <li>• PEF 33 - 50% best or predicted</li> <li>• Can't complete sentences</li> <li>• RR &gt; 25/min</li> <li>• Pulse &gt; 110 bpm</li> </ul>	<ul style="list-style-type: none"> <li>• PEF &lt; 33% best or predicted</li> <li>• Oxygen sats &lt; 92%</li> <li>• Silent chest, cyanosis or feeble respiratory effort</li> <li>• Bradycardia, dysrhythmia or hypotension</li> <li>• Exhaustion, confusion or coma</li> </ul>

### British Thoracic Society guidelines

- magnesium sulphate recommended as next step for patients who are not responding (e.g. 1.2 - 2g IV over 20 mins)
- little evidence to support use of IV aminophylline (although still mentioned in management plans)
- if no response consider IV salbutamol

A 31-year-old man with a history of asthma presents to the Emergency Department with dyspnoea not responding to his salbutamol inhaler. On examination he is noted to have reduced breath sounds on the right side and a chest x-ray confirms a pneumothorax with a 1.5cm rim of air. A pleural aspiration is performed and the patient's dyspnoea resolves. What advice should he be given before discharge?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Air travel should be avoided for the next 12 months  |
| <input type="radio"/> | B. His asthma treatment should be increased to the next step on the British Thoracic Society guidelines |
| <input type="radio"/> | C. Playing wind instruments such as the trombone should be avoided for the next 12 months               |
| <input type="radio"/> | D. Scuba diving should be avoided for life  |
| <input type="radio"/> | E. Vigorous exercise should be avoided for the next 3 months  |

Next question

This man has developed a secondary spontaneous pneumothorax. The British Thoracic Society (BTS) guidelines state: *'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'*

Air travel is acceptable once the pneumothorax has fully resolved.

## Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

### Primary pneumothorax

Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails (defined as > 2 cm or still short of breath) then a chest drain should be inserted

### Secondary pneumothorax

Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and/or the patient is short of breath then a chest drain should be inserted.

- otherwise aspiration should be attempted if the rim of air is between 1-2cm. If aspiration fails (i.e. pneumothorax is still greater than 1cm) a chest drain should be inserted. All patients should be admitted for at least 24 hours
- if the pneumothorax is less than 1cm then the BTS guidelines suggest giving oxygen and admitting for 24 hours
- regarding scuba diving, the BTS guidelines state: *'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'*

## **Iatrogenic pneumothorax**

Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
- majority will resolve with observation, if treatment is required then aspiration should be used
- ventilated patients need chest drains, as may some patients with COPD



Each one of the following is a risk factor for lung cancer, except:

<input type="radio"/>	A. Radon
<input type="radio"/>	B. Cryptogenic fibrosing alveolitis
<input type="radio"/>	C. Coal dust
<input type="radio"/>	D. Asbestos
<input type="radio"/>	E. Arsenic

Next question

### Lung cancer: risk factors

#### Smoking

- increases risk of lung ca by a factor of 10

#### Other factors

- asbestos - increases risk of lung ca by a factor of 5
- arsenic
- radon
- nickel
- chromate
- aromatic hydrocarbon
- cryptogenic fibrosing alveolitis

#### Factors that are NOT related

- coal dust

Smoking and asbestos are synergistic, i.e. a smoker with asbestos exposure has a  $10 * 5 = 50$  times increased risk

A 42-year-old woman presents with pyrexia and a productive cough. Around 10 days ago she developed symptoms consistent with a flu-like illness. For around 4-5 days she was in bed with myalgia, fever and lethargy. Initially there was an improvement in her condition but over the past three days she has developed a cough productive of thick pink-yellow sputum. On examination there are scattered crackles in the right base. Her symptoms are not severe enough to warrant admission and oral amoxicillin is prescribed. Which other medication should also be given?

<input type="radio"/>	A. Aciclovir
<input type="radio"/>	B. Ciprofloxacin
<input type="radio"/>	C. Oseltamivir
<input type="radio"/>	D. Flucloxacillin
<input type="radio"/>	E. Penicillin V

There is a high incidence of *Staphylococcus aureus* pneumonia in patients following influenza. As a result the BNF advises the co-prescription of flucloxacillin in such a situation.

### Pneumonia: community-acquired

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- *Staphylococcus aureus*: commonly after the 'flu
- atypical pneumonias (e.g. Due to *Mycoplasma pneumoniae*)
- viruses

*Klebsiella pneumoniae* is classically in alcoholics

***Streptococcus pneumoniae* (pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

### Management

The British Thoracic Society published guidelines in 2009:

- low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital
- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin

You review a 28-year-old woman with no past medical history of note. For the past week she has been experiencing left sided pleuritic chest pain. Her GP treated her for pleurisy with amoxicillin but there has been no improvement in her symptoms. She denies any shortness of breath and oxygen saturations on room air are 98%. A chest x-ray shows a 20% pneumothorax on the left side. What is the most appropriate management?

- ☐ A. Observe for 24 hours before discharging with standard advice
- ☐ B. Insert a chest drain
- ☐ C. Discharge with standard advice
- ☐ D. Aspiration
- ☐ E. Observe for 48 hours then repeat chest x-ray

[Next question](#)

Questions sometimes discuss the size of the pneumothorax in percentage terms rather than giving the interpleural distance. A variety of formulas have been proposed to convert between the two.

As a very general rule of thumb:

Average interpleural distance	Approximate size of pneumothorax
0.5 cm	10%
1 cm	15 %
2 cm	30%
3 cm	45%
4 cm	60%

A pneumothorax of 20% is therefore within the 2 cm limit suggested by the British Thoracic Society for observation, if the patient is not short of breath.

## Pneumothorax

The British Thoracic Society (BTS) published updated guidelines for the management of spontaneous pneumothorax in 2010. A pneumothorax is termed primary if there is no underlying lung disease and secondary if there is

### Primary pneumothorax

Recommendations include:

- if the rim of air is < 2cm and the patient is not short of breath then discharge should be considered
- otherwise aspiration should be attempted
- if this fails (defined as > 2 cm or still short of breath) then a chest drain should be inserted

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Recommendations include:

- if the patient is > 50 years old and the rim of air is > 2cm and/or the patient is short of breath then a chest drain should be inserted.
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- regarding scuba diving, the BTS guidelines state: *'Diving should be permanently avoided unless the patient has undergone bilateral surgical pleurectomy and has normal lung function and chest CT scan postoperatively.'*

## Iatrogenic pneumothorax

Recommendations include:

- less likelihood of recurrence than spontaneous pneumothorax
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- ventilated patients need chest drains, as may some patients with COPD

### Question 134 of 134

What is the mode of inheritance of alpha-1 antitrypsin deficiency?

- A. Mitochondrial
- B. X-linked recessive
- C. Polygenic
- D. Autosomal recessive**
- E. Autosomal dominant

Alpha-1 antitrypsin deficiency - autosomal recessive / co-dominant

Alpha-1 antitrypsin deficiency is also sometimes listed as being an autosomal co-dominant condition. Unfortunately trusted sources vary - how would you classify A1AT?

#### Alpha-1 antitrypsin deficiency

Alpha-1 antitrypsin (A1AT) deficiency is a common inherited condition caused by a lack of a protease inhibitor (Pi) normally produced by the liver. The role of A1AT is to protect cells from enzymes such as neutrophil elastase.

#### Genetics

- located on chromosome 14
- inherited in an autosomal recessive / co-dominant fashion\*
- alleles classified by their electrophoretic mobility - M for normal, S for slow, and Z for very slow
- normal = PiMM
- homozygous PiSS (50% normal A1AT levels)
- homozygous PiZZ (10% normal A1AT levels)

#### Features

- patients who manifest disease usually have PiZZ genotype
- lungs: panacinar emphysema, most marked in lower lobes
- liver: cirrhosis and hepatocellular carcinoma in adults, cholestasis in children

#### Investigations

- A1AT concentrations

## Management

- no smoking
- supportive: bronchodilators, physiotherapy
- intravenous alpha1-antitrypsin protein concentrates
- surgery: volume reduction surgery, lung transplantation

\*trusted sources are split on which is a more accurate description

**Question 1 of 151**

Next

A 54-year-old female presents with fatigue and xerostomia. Bloods tests reveal the following:

Hb	13.9 g/dl
WBC	6.1 *10 <sup>9</sup> /l
Platelets	246 *10 <sup>9</sup> /l
Bilirubin	33 µmol/l
ALP	292 u/l
ALT	47 u/l

What is the most likely diagnosis?

- ☐ A. Systemic lupus erythematosus
- ☐ B. Infectious mononucleosis
- ☐ C. Primary biliary cirrhosis
- ☐ D. Autoimmune hepatitis
- ☐ E. Primary Sjogren's syndrome

Next question

Primary biliary cirrhosis - the **M** rule

- **IgM**
- anti-**M**itochondrial antibodies, **M2** subtype
- **M**iddle aged females

The dry mouth in this patient is due to sicca syndrome, which occurs in 70% of cases of primary biliary cirrhosis. The raised alkaline phosphatase points towards a diagnosis of primary biliary cirrhosis rather than primary Sjogren's syndrome.

**Primary biliary cirrhosis: features**

Primary biliary cirrhosis is a chronic liver disorder typically seen in middle-aged females (female:male ratio of 9:1). The aetiology is not fully understood although it is thought to be an autoimmune condition. Interlobular bile ducts become damaged by a chronic inflammatory process causing progressive cholestasis, which may eventually progress to cirrhosis. The classic presentation is itching in a middle-aged woman.

Clinical features

- early: may be asymptomatic (e.g. raised ALP on routine LFTs) or fatigue, pruritus
- cholestatic jaundice
- hyperpigmentation, especially over pressure points
- xanthelasmas, xanthomata
- also: clubbing, hepatosplenomegaly
- late: may progress to liver failure

## Complications

- malabsorption: osteomalacia, coagulopathy
- sicca syndrome occurs in 70% of cases
- portal hypertension: ascites, variceal haemorrhage
- hepatocellular cancer (20-fold increased risk)



Which one of the following is the most likely presentation of *Staphylococcus aureus* food poisoning?

- ☐ A. Tenesmus
- ☐ B. Watery diarrhoea
- ☐ C. Dysentery
- ☐ D. Severe vomiting
- ☐ E. Presentation 24-48 hours after eating affected food

Next question

Severe nausea and vomiting are caused by enterotoxins A-E

### Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

### Stereotypical histories

<b><i>Escherichia coli</i></b>	Common amongst travellers Watery stools Abdominal cramps and nausea
<b>Giardiasis</b>	Prolonged, non-bloody diarrhoea
<b>Cholera</b>	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
<b><i>Shigella</i></b>	Bloody diarrhoea Vomiting and abdominal pain
<b><i>Staphylococcus aureus</i></b>	Severe vomiting Short incubation period
<b><i>Campylobacter</i></b>	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody

	Complications include Guillain-Barre syndrome
<b><i>Bacillus cereus</i></b>	Two types of illness are seen <ul style="list-style-type: none"> <li>• vomiting within 6 hours, stereotypically due to rice</li> <li>• diarrhoeal illness occurring after 6 hours</li> </ul>
<b>Amoebiasis</b>	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

#### Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus*\*
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

\*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

### Question 3 of 151

Next

Which one of the following is most suggestive of Wilson's disease?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Reduced hepatic copper concentration  |
| <input type="radio"/> | B. Reduced 24hr urinary copper excretion |
| <input type="radio"/> | C. Increased skin pigmentation           |
| <input type="radio"/> | D. Reduced serum caeruloplasmin          |
| <input type="radio"/> | E. Reduced serum copper                  |

Next question

Wilson's disease - serum caeruloplasmin is **decreased**

### Wilson's disease

Wilson's disease is an autosomal recessive disorder characterised by excessive copper deposition in the tissues. Metabolic abnormalities include increased copper absorption from the small intestine and decreased hepatic copper excretion. Wilson's disease is caused by a defect in the ATP7B gene located on chromosome 13

The onset of symptoms is usually between 10 - 25 years. Children usually present with liver disease whereas the first sign of disease in young adults is often neurological disease

Features result from excessive copper deposition in the tissues, especially the brain, liver and cornea:

- liver: hepatitis, cirrhosis
- neurological: speech and behavioural problems are often the first manifestations. Also: excessive salivation, tremor, chorea
- Kayser-Fleischer rings
- renal tubular acidosis (esp. Fanconi syndrome)
- haemolysis
- blue nails

### Diagnosis

- reduced serum caeruloplasmin
- increased 24hr urinary copper excretion

## Management

- penicillamine (chelates copper) has been the traditional first-line treatment
- trientine hydrochloride is an alternative chelating agent which may become first-line treatment in the future
- tetrathiomolybdate is a newer agent that is currently under investigation

#### Question 4 of 151

Next

A 54-year-old man with a long history of heartburn has an endoscopy to investigate his symptoms. A biopsy is taken from an abnormal area of mucosa in the lower oesophagus and reported as follows:

Non-dysplastic columnar-lined oesophagus

What is the most suitable management?

<input type="radio"/>	A. Reassure and discharge
<input type="radio"/>	B. Fundoplication
<input type="radio"/>	C. Laser ablation
<input type="radio"/>	D. Ivor-Lewis oesophagectomy
<input type="radio"/>	E. High-dose proton pump inhibitor and follow-up

Next question

The 2005 British Society of Gastroenterology guidelines state that high-dose proton pump inhibitor therapy is first-line treatment in such patients. There is yet insufficient evidence to support the use of endoscopic ablation.

#### Barrett's oesophagus

Barrett's refers to the metaplasia of the lower oesophageal mucosa, with the usual squamous epithelium being replaced by columnar epithelium. There is an increased risk of oesophageal adenocarcinoma, estimated at 50-100 fold.

Histological features

- the columnar epithelium may resemble that of either the cardiac region of the stomach or that of the small intestine (e.g. with goblet cells, brush border)

Management

- endoscopic surveillance with biopsies
- high-dose proton pump inhibitor

### Question 5 of 151

Next

A 46-year-old man is being investigated for indigestion. Jejunal biopsy shows deposition of macrophages containing PAS-positive granules. What is the most likely diagnosis?

- |                       |                         |
|-----------------------|-------------------------|
| <input type="radio"/> | A. Bacterial overgrowth |
| <input type="radio"/> | B. Coeliac disease      |
| <input type="radio"/> | C. Tropical sprue       |
| <input type="radio"/> | D. Whipple's disease    |
| <input type="radio"/> | E. Small bowel lymphoma |

Next question

Whipple's disease: jejunal biopsy shows deposition of macrophages containing Periodic acid-Schiff (PAS) granules

### Whipple's disease

Whipple's disease is a rare multi-system disorder caused by *Tropheryma whippelii* infection. It is more common in those who are HLA-B27 positive and in middle-aged men

#### Features

- malabsorption: diarrhoea, weight loss
- large-joint arthralgia
- lymphadenopathy
- skin: hyperpigmentation and photosensitivity
- pleurisy, pericarditis
- neurological symptoms (rare): ophthalmoplegia, dementia, seizures, ataxia, myoclonus

#### Investigation

- jejunal biopsy shows deposition of macrophages containing Periodic acid-Schiff (PAS) granules

#### Management

- varies e.g. IV penicillin then oral co-trimoxazole for a year

A 31-year-old man with a known history of alcoholic liver disease is reviewed following a suspected oesophageal variceal haemorrhage. He has been resuscitated and intravenous terlipressin has been given. His blood pressure is now 104/60 mmHg and his pulse is 84/min. What is the most appropriate intervention?

<input type="radio"/>	A. Transjugular Intrahepatic Portosystemic Shunt
<input type="radio"/>	B. Surgical referral
<input type="radio"/>	C. Endoscopic variceal band ligation
<input type="radio"/>	D. Sengstaken-Blakemore tube
<input type="radio"/>	E. Endoscopic sclerotherapy

[Next question](#)

## Oesophageal varices

### Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent and is supported by NICE guidelines. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy. NICE recommend band ligation
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

### Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

A 25-year-old man presents with lethargy and increased skin pigmentation. Blood test reveal deranged liver function tests and impaired glucose tolerance. Given the likely diagnosis of haemochromatosis, what is the most appropriate initial investigation strategy?

<input type="radio"/>	A. Transferrin saturation + ferritin
<input type="radio"/>	B. Haematocrit + ferritin
<input type="radio"/>	C. Liver biopsy with Perl's stain
<input type="radio"/>	D. Serum iron + ferritin
<input type="radio"/>	E. Serum iron + haematocrit

[Next question](#)

#### Screening for haemochromatosis

- general population: transferrin saturation > ferritin
- family members: HFE genetic testing

The British Committee for Standards in Haematology (BCSH) guidelines recommend measuring the transferrin saturation first as this is the most specific and sensitive test for iron accumulation. They also recommend that serum ferritin is measured but this marker is not usually abnormal in the early stages of iron accumulation

#### Haemochromatosis: investigation

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6\*. The British Committee for Standards in Haematology (BCSH) published guidelines for the investigation and management of haemochromatosis in 2000

There is continued debate about the best investigation to screen for haemochromatosis. The 2000 BCSH guidelines suggest:

- general population: transferrin saturation is considered the most useful marker. Ferritin should also be measured but is not usually abnormal in the early stages of iron accumulation
- testing family members: genetic testing for HFE mutation

These guidelines may change as HFE gene analysis become less expensive

#### Diagnostic tests

- molecular genetic testing for the C282Y and H63D mutations



- liver biopsy: Perl's stain

Typical iron study profile in patient with haemochromatosis

- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

Monitoring adequacy of venesection

- BSCH recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Joint x-rays characteristically show chondrocalcinosis

\*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

**Question 8 of 151**

Next

A patient with upper gastrointestinal symptoms tests positive for *Helicobacter pylori* following a urea breath test. Which one of the following conditions is most strongly associated *Helicobacter pylori* infection?

<input type="radio"/>	A. Gastric adenocarcinoma
<input type="radio"/>	B. Gastro-oesophageal reflux disease
<input type="radio"/>	C. Oesophageal cancer
<input checked="" type="radio"/>	D. Duodenal ulceration
<input type="radio"/>	E. Atrophic gastritis

Next question

*Helicobacter pylori* infection is also associated with both gastric adenocarcinoma and atrophic gastritis but the strongest association is with duodenal ulceration.

***Helicobacter pylori***

*Helicobacter pylori* is a Gram negative bacteria associated with a variety of gastrointestinal problems, principally peptic ulcer disease

**Associations**

- peptic ulcer disease (95% of duodenal ulcers, 75% of gastric ulcers)
- gastric cancer
- B cell lymphoma of MALT tissue (eradication of H pylori results causes regression in 80% of patients)
- atrophic gastritis

The role of H pylori in Gastro-oesophageal reflux disease (GORD) is unclear - there is currently no role in GORD for the eradication of H pylori

Management - eradication may be achieved with a 7 day course of

- a proton pump inhibitor + amoxicillin + clarithromycin, or
- a proton pump inhibitor + metronidazole + clarithromycin

A 24-year-old man presents with rectal bleeding and pain on defecation. This has been present for the past two weeks. He has a tendency towards constipation and notices that when he wipes himself fresh blood is often on the paper. Rectal examination is limited due to pain but no external abnormalities are seen. What is the most likely diagnosis?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Internal haemorrhoids |
| <input type="radio"/> | B. Anal carcinoma        |
| <input type="radio"/> | C. Rectal polyp          |
| <input type="radio"/> | D. Anogenital herpes     |
| <input type="radio"/> | E. Anal fissure          |

[Next question](#)

Superficial anal fissures may be difficult to see on examination.

### Anal fissure

Anal fissures are longitudinal or elliptical tears of the squamous lining of the distal anal canal. If present for less than 6 weeks they are defined as acute, and chronic if present for more than 6 weeks. Around 90% of anal fissures occur on the posterior midline

Management of an acute anal fissure (< 6 weeks)

- dietary advice: high-fibre diet with high fluid intake
- bulk-forming laxatives are first line - if not tolerated then lactulose should be tried
- lubricants such as petroleum jelly may be tried before defecation
- topical anaesthetics

-analgesia

- topical steroids do not provide significant relief

Management of a chronic anal fissure (> 6 weeks)

- the above techniques should be continued
- topical glyceryl trinitrate (GTN) is first line treatment for a chronic anal fissure
- if topical GTN is not effective after 8 weeks then secondary referral should be considered for surgery or botulinum toxin

**Question 10 of 151**

Next

A 54-year-old woman presents with jaundice shortly after being discharged from hospital. Liver function tests are reported as follows:

Albumin	49 g/l
Bilirubin	89 µmol/l
Alanine transferase (ALT)	66 iu/l
Alkaline phosphatase (ALP)	245 µmol/l
Gamma glutamyl transferase (γGT)	529 u/l

Which of the following antibiotics is she most likely to have received?

- ☐ A. Flucloxacillin
- ☐ B. Gentamicin
- ☐ C. Ciprofloxacin
- ☐ D. Trimethoprim
- ☐ E. Ceftazidime

Next question

Flucloxacillin + co-amoxiclav are well recognised causes of cholestasis

**Drug-induced liver disease**

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol

- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin\*, nitrofurantoin
- anabolic steroids, testosterone
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

\*risk may be reduced with erythromycin stearate

A 43-year-old man presents with diarrhoea and rectal bleeding for the past ten days. On examination he has brown pigmented lesions on his lips and palms but abdominal and rectal examination is unremarkable. What is the most likely cause for this presentation?

<input type="radio"/>	A. Intussusception
<input type="radio"/>	B. Angiodysplasia
<input type="radio"/>	C. Meckel's Diverticulum
<input checked="" type="radio"/>	D. Colon cancer
<input type="radio"/>	E. Diverticular abscess

[Next question](#)

This patient has Peutz-Jeghers syndrome. Intussusception would not normally cause rectal bleeding at this age. Colon cancer is the most common type of gastrointestinal cancer that patients with Peutz-Jeghers syndrome develop.

### Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

#### Genetics

- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

#### Features

- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

#### Management

- conservative unless complications develop

**Question 12 of 151**

Next

A 54-year-old female presents with a 3 month history of dysphagia affecting both food and liquids from the start, along with occasional symptoms of heartburn. What is the most likely underlying diagnosis?

<input type="radio"/>	A. Pharyngeal pouch
<input type="radio"/>	B. Gastric adenocarcinoma
<input type="radio"/>	C. Benign stricture
<input type="radio"/>	D. Oesophageal cancer
<input type="radio"/>	E. Achalasia

Next question

Dysphagia affecting both solids and liquids from the start - think achalasia

This is a classic history of achalasia with dysphagia affecting both solids and liquids from the start.

**Achalasia**

Failure of oesophageal peristalsis and of relaxation of lower oesophageal sphincter (LOS) due to degenerative loss of ganglia from Auerbach's plexus i.e. LOS contracted, oesophagus above dilated. Achalasia typically presents in middle-age and is equally common in men and women.

**Clinical features**

- dysphagia of BOTH liquids and solids
- typically variation in severity of symptoms
- heartburn
- regurgitation of food - may lead to cough, aspiration pneumonia etc
- malignant change in small number of patients

**Investigations**

- manometry: excessive LOS tone which doesn't relax on swallowing - considered most important diagnostic test
- barium swallow shows grossly expanded oesophagus, fluid level
- CXR: wide mediastinum, fluid level

**Treatment**

- intra-sphincteric injection of botulinum toxin
- Heller cardiomyotomy
- balloon dilation
- drug therapy has a role but is limited by side-effects

**Question 13 of 151**

Next

A 22-year-old male blood donor is noted to have the following blood results:

Bilirubin	41 µmol/L
ALP	84 U/L
ALT	23 U/L
Albumin	41 g/L
Dipstick urinalysis	No bilirubinuria

He has recently complained of coryzal symptoms and a non-productive cough. What is the most likely diagnosis?

- ☐ A. Gilbert's syndrome
- ☐ B. Dubin-Johnson syndrome
- ☐ C. Rotor syndrome
- ☐ D. Hepatitis C infection
- ☐ E. Infectious mononucleosis

Next question

An isolated hyperbilirubinaemia in a 22-year-old male is likely to be secondary to Gilbert's syndrome. The normal dipstick urinalysis excludes Dubin-Johnson and Rotor syndrome as these both produce a conjugated bilirubinaemia. Viral infections are common triggers for a rise in the bilirubin in patients with Gilbert's

**Gilbert's syndrome**

Gilbert's syndrome is an autosomal recessive\* condition of defective bilirubin conjugation due to a deficiency of UDP glucuronyl transferase. The prevalence is approximately 1-2% in the general population

**Features**

- unconjugated hyperbilirubinaemia (i.e. not in urine)
- jaundice may only be seen during an intercurrent illness

**Investigation and management**

- investigation: rise in bilirubin following prolonged fasting or IV nicotinic acid
- no treatment required

\*the exact mode of inheritance is still a matter of debate



**Question 14 of 151**

Next

A 55-year-old man with a history of gallstone disease presents with a two day history of pain in the right upper quadrant. He has feels 'like I have flu' and his wife reports he has had a fever for the past day. On examination his temperature is 38.1°C, blood pressure 100/60 mmHg, pulse 102/min and he is tender in the right upper quadrant. His sclera have a yellow-tinge. What is the most likely diagnosis?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Pancreatic cancer     |
| <input type="radio"/> | B. Biliary colic         |
| <input type="radio"/> | C. Ascending cholangitis |
| <input type="radio"/> | D. Acute cholecystitis   |
| <input type="radio"/> | E. Acute viral hepatitis |

Next question

This patient has Charcot's triad (right upper quadrant pain, fever and jaundice), which is classically linked to ascending cholangitis. The systemic upset and jaundice are less typical of acute cholecystitis.

**Ascending cholangitis**

Ascending cholangitis is a bacterial infection of the biliary tree. The most common predisposing factor is gallstones.

Charcot's triad of right upper quadrant (RUQ) pain, fever and jaundice occurs in about 20-50% of patients

- fever is the most common feature, seen in 90% of patients
- RUQ pain 70%
- jaundice 60%
- hypotension and confusion are also common

**Management**

- intravenous antibiotics
- endoscopic retrograde cholangiopancreatography (ERCP) after 24-48 hours to relieve any obstruction

Of the following, which one is the most useful prognostic marker in paracetamol overdose?

<input type="radio"/>	A. ALT
<input type="radio"/>	B. Prothrombin time
<input type="radio"/>	C. Paracetamol levels at presentation
<input type="radio"/>	D. Paracetamol levels at 12 hours
<input type="radio"/>	E. Paracetamol levels at 24 hours

Next question

An elevated prothrombin time signifies liver failure in paracetamol overdose and is a marker of poor prognosis. However, arterial pH, creatinine and encephalopathy are also markers of a need for liver transplantation

### Paracetamol overdose: management

#### Management

The following is based on the current BNF guidance. The National Poisons Information Service/TOXBASE should always be consulted for situations outside of the normal parameters.

Activated charcoal should be given if:

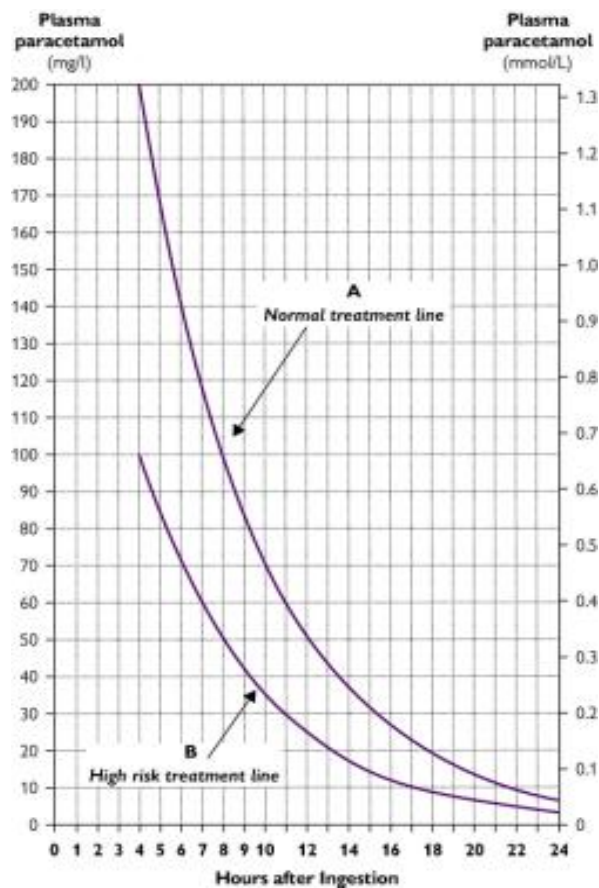
- paracetamol dose is in excess of 150 mg/kg (75 mg/kg if high-risk, see below) or 12 g, whichever is the smaller, and;
- the paracetamol was ingested in the previous hour

Patients presenting within 8 hours

- paracetamol levels (along with U&Es, LFTs and prothrombin time) should be checked 4 hours after ingestion (earlier samples may be misleading)
- the value should be plotted on a paracetamol treatment graph (see below)
- if the value is above the relevant treatment line intravenous acetylcysteine should be given

Patients presenting 8-24 hours after ingestion

- take an immediate blood sample for paracetamol levels, U&Es, LFTs and prothrombin time
- start acetylcysteine immediately if it is thought that more than 150 mg/kg body weight has been ingested. If the high risk (see below) consider treatment at a lower dose (75 mg/kg)
- otherwise wait for the paracetamol level, give intravenous acetylcysteine if the value is above the relevant treatment line



The following groups of patients are at an increased risk of developing hepatotoxicity following a paracetamol overdose and hence are considered 'high-risk':

- patients taking liver enzyme-inducing drugs (rifampicin, phenytoin, carbamazepine, chronic alcohol excess, St John's Wort)
- malnourished patients (e.g. anorexia or bulimia, cystic fibrosis, hepatitis C, alcoholism, HIV)
- patients who have not eaten for a few days

#### King's College Hospital criteria for liver transplantation (paracetamol liver failure)

Arterial pH < 7.3, 24 hours after ingestion

or all of the following:

- prothrombin time > 100 seconds
- creatinine > 300  $\mu\text{mol/l}$
- grade III or IV encephalopathy

## Question 16 of 151

Next

A 49-year-old female is referred to the gastroenterology out-patient clinic with a 3 month history of epigastric pain and diarrhoea. Her GP initially prescribed lansoprazole 30mg od but this didn't alleviate her symptoms. The only past medical history of note is hyperparathyroidism.

Endoscopy revealed multiple duodenal ulcerations. What is the likely diagnosis?

<input type="radio"/>	A. Multiple endocrine neoplasia type II a
<input type="radio"/>	B. Coeliac disease
<input type="radio"/>	C. Multiple endocrine neoplasia type I
<input type="radio"/>	D. Autoimmune polyendocrinopathy syndrome
<input type="radio"/>	E. Crohn's disease

Next question

Zollinger-Ellison syndrome: epigastric pain and diarrhoea

Zollinger-Ellison syndrome typically presents with multiple gastroduodenal ulcers causing abdominal pain and diarrhoea. High-dose proton pump inhibitors are needed to control the symptoms. Around a third of patients may have multiple endocrine neoplasia type I (MEN-I), explaining the hyperparathyroidism in this patient.

### MEN-I

- parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia
- pituitary (70%)
- pancreas (50%, e.g. Insulinoma, gastrinoma)
- also: adrenal and thyroid

### Zollinger-Ellison syndrome

Zollinger-Ellison syndrome is condition characterised by excessive levels of gastrin, usually from a gastrin secreting tumour usually of the duodenum or pancreas. Around 30% occur as part of MEN type I syndrome

### Features

- multiple gastroduodenal ulcers
- diarrhoea
- malabsorption

### Diagnosis

- fasting gastrin levels: the single best screen test
- secretin stimulation test

A 35-year-old man who is usually fit and well presents with a 2 month history of indigestion. His weight is stable and there is no history of dysphagia. Examination of the abdomen is unremarkable. Of the following options, what is the most suitable initial management?

<input type="radio"/>	A. Urea breath testing and non-urgent referral for endoscopy
<input type="radio"/>	B. H pylori eradication therapy and full-dose proton pump inhibitor for three months
<input type="radio"/>	C. Full-dose Proton pump inhibitor and immediate referral for endoscopy
<input type="radio"/>	D. Three month course of a standard-dose proton pump inhibitor
<input type="radio"/>	E. One month course of a full-dose proton pump inhibitor

[Next question](#)

This question highlights the NICE guidelines for the management of dyspepsia.

There is no evidence currently to suggest whether a one month course of a PPI or 'test and treat' strategy should be adopted first line. Many clinicians prefer to test for H pylori first as this cannot be done within 2 weeks of acid-suppression therapy, as false-negative results may occur

Given the options available, only the answer is in line with current NICE guidelines

### Dyspepsia

In 2004 NICE published guidelines for the management of dyspepsia in primary care. These take into account the age of the patient (whether younger or older than 55 years) and the presence or absence of 'alarm signs':

- chronic gastrointestinal bleeding
- progressive unintentional weight loss
- progressive difficulty swallowing
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal

### Deciding whether urgent referral for endoscopy is needed

Urgent referral (within 2 weeks) is indicated for patients with any alarm signs irrespective of age

Routine endoscopic investigation of patients of any age, presenting with dyspepsia and without alarm signs is not necessary, however

Patients aged 55 years and over should be referred urgently for endoscopy if dyspepsia symptoms are:

- recent in onset rather than recurrent and
- unexplained (e.g. New symptoms which cannot be explained by precipitants such as NSAIDs) and
- persistent: continuing beyond a period that would normally be associated with self-limiting problems (e.g. Up to four to six weeks, depending on the severity of signs and symptoms)

### **Managing patients who do not meet referral criteria ('undiagnosed dyspepsia')**

This can be summarised at a step-wise approach

1. Review medications for possible causes of dyspepsia
2. Lifestyle advice
3. Trial of full-dose PPI for one month\*
4. 'Test and treat' using carbon-13 urea breath test

\*it is unclear from studies whether a trial of a PPI or a 'test and treat' should be used first

A 38-year-old female with a long history of alcohol excess presents with abdominal pain, weight loss and bulky stools. What is the most suitable investigation to confirm the diagnosis?

<input type="radio"/>	A. Endoscopic ultrasound
<input type="radio"/>	B. Endoscopic retrograde cholangiopancreatography
<input type="radio"/>	C. Ultrasound abdomen
<input type="radio"/>	D. CT abdomen
<input type="radio"/>	E. Endoscopy with D2 biopsy

[Next question](#)

This patient has chronic pancreatitis. CT is the most sensitive method to detect the characteristic pancreatic calcification which is associated with the condition

### Chronic pancreatitis

Chronic pancreatitis is an inflammatory condition which can ultimately affect both the exocrine and endocrine functions of the pancreas. Around 80% of cases are due to alcohol excess with up to 20% of cases being unexplained

#### Features

- pain is typically worse 15 to 30 minutes following a meal
- steatorrhea: symptoms of pancreatic insufficiency usually develop between 5 and 25 years after the onset of pain
- diabetes mellitus develops in the majority of patients. It typically occurs more than 20 years after symptom begin

#### Investigation

- abdominal x-ray shows pancreatic calcification in 30% of cases
- CT is more sensitive at detecting pancreatic calcification. Sensitivity is 80%, specificity is 85%
- functional tests: faecal elastase may be used to assess exocrine function if imaging inconclusive

#### Management

- pancreatic enzyme supplements
- analgesia
- antioxidants: limited evidence base - one study suggests benefit in early disease

**Question 19 of 151**

Next

A 54-year-old man is investigated for dyspepsia. An endoscopy shows a gastric ulcer and a CLO test done during the procedure demonstrates *H. pylori* infection. A course of *H. pylori* eradication therapy is given. Six weeks later the patient comes for review. What is the most appropriate test to confirm eradication?

<input type="radio"/>	A. Culture of gastric biopsy
<input type="radio"/>	B. <i>H. pylori</i> serology
<input type="radio"/>	C. Hydrogen breath test
<input type="radio"/>	D. Urea breath test
<input type="radio"/>	E. Stool culture

Next question

It is important to remember that *H. pylori* serology remains positive following eradication

***Helicobacter pylori*: tests****Urea breath test**

- patients consume a drink containing carbon isotope 13 (<sup>13</sup>C) enriched urea
- urea is broken down by *H. pylori* urease
- after 30 mins patient exhale into a glass tube
- mass spectrometry analysis calculates the amount of <sup>13</sup>C CO<sub>2</sub>
- should not be performed within 4 weeks of treatment with an antibacterial or within 2 weeks of an antisecretory drug (e.g. a proton pump inhibitor)
- sensitivity 95-98%, specificity 97-98%

**Rapid urease test (e.g. CLO test)**

- biopsy sample is mixed with urea and pH indicator
- colour change if *H. pylori* urease activity
- sensitivity 90-95%, specificity 95-98%

**Serum antibody**

- remains positive after eradication
- sensitivity 85%, specificity 80%

**Culture of gastric biopsy**

- provide information on antibiotic sensitivity
- sensitivity 70%, specificity 100%



### Gastric biopsy

- histological evaluation alone, no culture
- sensitivity 95-99%, specificity 95-99%

### Stool antigen test

- sensitivity 90%, specificity 95%

A 34-year-old female with a history of alcoholic liver disease is admitted with frank haematemesis. She was discharged three months ago following treatment for bleeding oesophageal varices. Following resuscitation, what is the most appropriate treatment whilst awaiting endoscopy?

<input type="radio"/>	A. Octreotide
<input type="radio"/>	B. Omeprazole
<input type="radio"/>	C. Propranolol
<input type="radio"/>	D. Tranexamic acid
<input type="radio"/>	E. Terlipressin

[Next question](#)

Terlipressin is the only licensed vasoactive agent for variceal haemorrhage in the UK

### Oesophageal varices

#### Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent and is supported by NICE guidelines. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy. NICE recommend band ligation
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

#### Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

**Question 21 of 151**

Next

Each one of the following is a risk factor for gastric cancer, except:

<input type="radio"/>	A. Smoking
<input type="radio"/>	B. Blood group O
<input type="radio"/>	C. Nitrates in diet
<input type="radio"/>	D. Pernicious anaemia
<input type="radio"/>	E. <i>H. pylori</i> infection

Next question

**Gastric cancer**

## Epidemiology

- overall incidence is decreasing, but incidence of tumours arising from the cardia is increasing
- peak age = 70-80 years
- more common in Japan, China, Finland and Colombia than the West
- more common in males, 2:1

## Associations

- *H. pylori* infection
- blood group A: gAstric cAncer
- gastric adenomatous polyps
- pernicious anaemia
- smoking
- diet: salty, spicy, nitrates
- may be negatively associated with duodenal ulcer

## Investigation

- diagnosis: endoscopy with biopsy
- staging: CT or endoscopic ultrasound - endoscopic ultrasound has recently been shown to be superior to CT

Crohn's disease is associated with each one of the following findings, except:

<input type="radio"/>	A. Inflammation confined to the mucosa and submucosa
<input type="radio"/>	B. Non-caseating granulomas
<input type="radio"/>	C. Rose-thorn ulcers
<input type="radio"/>	D. Cobblestone pattern
<input type="radio"/>	E. Fistulas

Next question

### IBD: histology

This histological differences between ulcerative colitis and Crohn's are summarised below:

#### Ulcerative colitis

- inflammation in mucosa and submucosa only (unless fulminant disease)
- widespread ulceration with preservation of adjacent mucosa which has the appearance of polyps ('pseudopolyps')
- inflammatory cell infiltrate in lamina propria
- crypt abscesses
- depletion of goblet cells and mucin from gland epithelium
- granulomas are infrequent

#### Crohn's

- inflammation occurs in all layers, down to the serosa. This predisposes to strictures, fistulas and adhesions
- oedema of mucosa and submucosa, combined with deep fissured ulcers ('rose-thorn') leads to a 'cobblestone' pattern
- lymphoid aggregates
- non-caseating granulomas

Which one of the following is most associated with the development of acute pancreatitis?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Hyperchylomicronaemia  |
| <input type="radio"/> | B. Amyloidosis            |
| <input type="radio"/> | C. Hypogammaglobulinaemia |
| <input type="radio"/> | D. Hypercholesterolaemia  |
| <input type="radio"/> | E. Hypotriglyceridaemia   |

Next question

Hyperchylomicronaemia may be caused by hereditary lipoprotein lipase deficiency and apolipoprotein CII deficiency. It predisposes to recurrent attacks of acute pancreatitis

### Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RPC
- **D**rugs (azathioprine, mesalazine\*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

\*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

**Question 24 of 151**

Next

A 42-year-old dentist is reviewed in the medical clinic complaining of persistent lethargy. Routine bloods show abnormal liver function tests so a hepatitis screen is sent. The results are shown below:

Anti-HAV IgG	negative
HBsAg	negative
Anti-HBs	positive
Anti-HBc	negative
Anti-HCV	positive

What do these results most likely demonstrate?

- ☐ A. Hepatitis B infection
- ☐ B. Hepatitis C infection
- ☐ C. Previous vaccination to hepatitis B and C
- ☐ D. Hepatitis C infection with previous hepatitis B vaccination
- ☐ E. Hepatitis B and C infection

Next question

Given the deranged liver function tests these results most likely indicate previous hepatitis B vaccination with active hepatitis C infection. However, around 15% of patients exposed to the hepatitis C virus clear the infection. It would therefore be necessary to perform a HCV PCR to see if the virus is still present

There is currently no vaccination for hepatitis C

**Hepatitis C**

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

**Transmission**

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

**Features**

- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

## Complications

- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

## Management of chronic infection

- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains
- the aim of treatment is sustained virological response (SVR), defined as undetectable

serum HCV RNA six months after the end of therapy

## Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

A 25-year-old man with a history of Crohn's disease is reviewed in clinic. Over the past week he has developed painful perianal ulcers. On examination numerous shallow ulcers can be seen with a small number of skin tags. What is the most appropriate first-line treatment?

<input type="radio"/>	A. Topical mesalazine
<input type="radio"/>	B. Oral metronidazole
<input type="radio"/>	C. Barrier creams + laxatives
<input type="radio"/>	D. Oral prednisolone
<input type="radio"/>	E. Oral mesalazine

Please see the British Society of Gastroenterology guidelines for more details.

### Crohn's disease: management

Crohn's disease is a form of inflammatory bowel disease. It commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus

#### General points

- patients should be strongly advised to stop smoking
- some studies suggest an increased risk of relapse secondary to NSAIDs and the combined oral contraceptive pill but the evidence is patchy

#### Active disease

- mesalazine: whilst evidence base is limited widely used in active disease
- steroids (oral, topical or intravenous)
- azathioprine is used as a second-line treatment in active disease
- methotrexate is used in patients intolerant of azathioprine or refractory disease. Usually given intramuscularly
- infliximab is useful in refractory disease and fistulating Crohn's. Patients typically continue on azathioprine or methotrexate

#### Perianal disease

- metronidazole is first-line

#### Enteral feeding with an elemental diet

- may be used in addition to or instead of other measures to induce remission

#### Surgery

- around 80% of patients with Crohn's disease will eventually have surgery



Which one of the following medications is least associated with dyspepsia?

<input type="radio"/>	A. Isosorbide mononitrate
<input type="radio"/>	B. Prednisolone
<input type="radio"/>	C. Aminophylline
<input checked="" type="radio"/>	D. Atenolol
<input type="radio"/>	E. Amlodipine

Next question

### Drugs causing dyspepsia

#### Causes

- NSAIDs
- bisphosphonates
- steroids

The following drugs may cause reflux by reducing lower oesophageal sphincter (LOS) pressure

- calcium channel blockers\*
- nitrates\*
- theophyllines

\*calcium channel blockers and nitrates are occasionally used in the management of achalasia, itself a cause of dyspepsia, because of their effect on the LOS.

A 23-year-old man develops watery diarrhoea 5 days after arriving in Mexico. Which one of the following is the most likely responsible organism?

- ☐ A. *Salmonella*
- ☐ B. *Shigella*
- ☐ C. *Campylobacter*
- ☐ D. *Escherichia coli*
- ☐ E. *Bacillus cereus*

[Next question](#)

*E. coli* is the most common cause of travellers' diarrhoea

## Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

## Stereotypical histories

<b><i>Escherichia coli</i></b>	Common amongst travellers Watery stools Abdominal cramps and nausea
<b>Giardiasis</b>	Prolonged, non-bloody diarrhoea
<b>Cholera</b>	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
<b><i>Shigella</i></b>	Bloody diarrhoea Vomiting and abdominal pain
<b><i>Staphylococcus aureus</i></b>	Severe vomiting

	Short incubation period
<b><i>Campylobacter</i></b>	<p>A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody</p> <p>Complications include Guillain-Barre syndrome</p>
<b><i>Bacillus cereus</i></b>	<p>Two types of illness are seen</p> <ul style="list-style-type: none"> <li>• vomiting within 6 hours, stereotypically due to rice</li> <li>• diarrhoeal illness occurring after 6 hours</li> </ul>
<b>Amoebiasis</b>	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

#### Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus*\*
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

\*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

**Question 28 of 151**

Next

A 44-year-old man is diagnosed with a duodenal ulcer. CLO testing performed during the gastroscopy is positive for *Helicobacter pylori*. What is the most appropriate management to eradicate *Helicobacter pylori*?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Lansoprazole + clindamycin + metronidazole  |
| <input type="radio"/> | B. Lansoprazole + amoxicillin + clindamycin    |
| <input type="radio"/> | C. Lansoprazole + amoxicillin + clarithromycin |
| <input type="radio"/> | D. Omeprazole + amoxicillin + clindamycin      |
| <input type="radio"/> | E. Omeprazole + penicillin + metronidazole     |

Next question

*H. pylori* eradication:

- PPI + amoxicillin + clarithromycin, or
- PPI + metronidazole + clarithromycin

The BNF recommends a regimen containing amoxicillin and clarithromycin as first-line therapy

***Helicobacter pylori***

*Helicobacter pylori* is a Gram negative bacteria associated with a variety of gastrointestinal problems, principally peptic ulcer disease

**Associations**

- peptic ulcer disease (95% of duodenal ulcers, 75% of gastric ulcers)
- gastric cancer
- B cell lymphoma of MALT tissue (eradication of H pylori results causes regression in 80% of patients)
- atrophic gastritis

The role of H pylori in Gastro-oesophageal reflux disease (GORD) is unclear - there is currently no role in GORD for the eradication of H pylori

Management - eradication may be achieved with a 7 day course of

- a proton pump inhibitor + amoxicillin + clarithromycin, or
- a proton pump inhibitor + metronidazole + clarithromycin

**Question 29 of 151**

Next

A 25-year-old woman develops deranged liver function tests following the introduction of a new drug. Alb 40, Bilirubin 46, ALT 576, ALP 95, γGT 150. Which of the following drugs is the most likely cause?

<input type="radio"/>	A. Oral contraceptive pill
<input type="radio"/>	B. Sodium valproate
<input type="radio"/>	C. Flucloxacillin
<input type="radio"/>	D. Chlorpromazine
<input type="radio"/>	E. Tetracycline

Next question

The liver function tests suggest a hepatitis rather than cholestasis. Sodium valproate may be associated with such a picture

**Drug-induced liver disease**

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin\*, nitrofurantoin
- anabolic steroids, testosterone
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

## Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

\*risk may be reduced with erythromycin stearate

Primary sclerosing cholangitis is most associated with:

<input type="radio"/>	A. Primary biliary cirrhosis
<input type="radio"/>	B. Crohn's disease
<input type="radio"/>	C. Hepatitis C infection
<input checked="" type="radio"/>	D. Ulcerative colitis
<input type="radio"/>	E. Coeliac disease

Next question

### Primary sclerosing cholangitis

Primary sclerosing cholangitis is a biliary disease of unknown aetiology characterised by inflammation and fibrosis of intra and extra-hepatic bile ducts

#### Associations

- ulcerative colitis: 4% of patients with UC have PSC, 80% of patients with PSC have UC
- Crohn's (much less common association than UC)
- HIV

#### Features

- cholestasis: jaundice and pruritus
- right upper quadrant pain
- fatigue

#### Investigation

- ERCP is the standard diagnostic tool, showing multiple biliary strictures giving a 'beaded' appearance
- ANCA may be positive
- there is a limited role for liver biopsy, which may show fibrous, obliterative cholangitis often described as 'onion skin'

#### Complications

- cholangiocarcinoma (in 10%)
- increased risk of colorectal cancer

Which one of the following is true regarding bacterial exotoxins?

<input type="radio"/>	A. They are mainly produced by Gram positive bacteria
<input type="radio"/>	B. Cholera toxin inhibits cAMP release in intestinal cells
<input type="radio"/>	C. Diphtheria toxin necrosis is limited to the pharynx, nasopharynx and tonsils
<input type="radio"/>	D. <i>Staph. aureus</i> exotoxins are not known to cause gastroenteritis
<input type="radio"/>	E. 'Lockjaw' seen in tetanus is secondary to blockade of the neuromuscular junction by Botulinus toxin

Next question

## Exotoxins and endotoxins

Exotoxins are secreted by bacteria where as endotoxins are only released following lysis of the cell.

### Exotoxins

Exotoxins are generally released by Gram positive bacteria with the notable exceptions of *Vibrio cholerae* and some strains of *E. coli*. There may be classified into a number of different groups:

Superantigens (bridge the MHC class II protein on antigen-presenting cells with the T cell receptor on the surface of T cells)

- *Staphylococcus aureus*: exotoxins lead to acute gastroenteritis (enterotoxins), toxic shock syndrome (TSST-1 superantigen) and staphylococcal scalded skin syndrome (exfoliatin)
- *Streptococcus pyogenes*: scarlet fever

AB toxins - ADP ribosylating

- diphtheria toxin inactivates elongation factor (EF-2) causing a 'diphtheric membrane' on tonsils caused by necrotic mucosal cells. Systemic distribution may produce necrosis of myocardial, neural and renal tissue.
- cholera toxin causes activation of adenylate cyclase leading to increases in cAMP levels, which in turn leads to increased chloride secretion
- pertussis exotoxin

Lockjaw is caused by *Clostridium tetani* neurotoxin (tetanospasmin)

### Endotoxins

Endotoxins are lipopolysaccharides that are released from Gram-negative bacteria such as *Neisseria meningitidis*.



**Question 32 of 151**

Next

A 76-year-old woman with a history of atrial fibrillation presents with abdominal pain and bloody diarrhoea. On examination her temperature is 37.8°C, pulse 102 / min and respiratory rate 30 / min. Her abdomen is tender with generalised guarding. Blood tests reveal the following:

Hb	10.9 g/dl
MCV	76 fl
Plt	348 * 10 <sup>9</sup> /l
WBC	23.4 * 10 <sup>9</sup> /l
Na <sup>+</sup>	141 mmol/l
K <sup>+</sup>	5.0 mmol/l
Bicarbonate	14 mmol/l
Urea	8.0 mmol/l
Creatinine	118 µmol/l

What is the most likely diagnosis?

<input type="radio"/>	A. Diverticulitis
<input type="radio"/>	B. Mesenteric ischaemia
<input type="radio"/>	C. <i>Campylobacter</i> infection
<input type="radio"/>	D. Ruptured abdominal aortic aneurysm
<input type="radio"/>	E. Ulcerative colitis

Next question

The low bicarbonate points to a metabolic acidosis - highly suggestive of mesenteric ischaemia.

**Mesenteric ischaemia**

Mesenteric ischaemia is primarily caused by arterial embolism resulting in infarction of the colon. It is more likely to occur in areas such as the splenic flexure that are located at the borders of the territory supplied by the superior and inferior mesenteric arteries.

**Predisposing factors**

- increasing age
- atrial fibrillation
- other causes of emboli: endocarditis
- cardiovascular disease risk factors: smoking, hypertension, diabetes

**Features**

- abdominal pain
- rectal bleeding
- diarrhoea
- fever
- bloods typically show an elevated WBC associated with acidosis

## Management

- supportive care
- laparotomy and bowel resection

**Question 33 of 151**

Next

A 65-year-old man with a history of dyspepsia is found to have a gastric MALT lymphoma on biopsy. What treatment should be offered?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Gastrectomy                  |
| <input type="radio"/> | B. Laser ablation               |
| <input type="radio"/> | C. None                         |
| <input type="radio"/> | D. CHOP chemotherapy            |
| <input type="radio"/> | E. <i>H. pylori</i> eradication |

Next question

Gastric MALT lymphoma - eradicate *H. pylori*

**Gastric MALT lymphoma**

## Overview

- associated with *H. pylori* infection in 95% of cases
- good prognosis
- if low grade then 80% respond to *H. pylori* eradication

## Features

- paraproteinaemia may be present

**Question 34 of 151**

Next

A 34-year-old HIV positive man is referred to gastroenterology due to jaundiced sclera. Liver function tests are as follows:

Albumin	34 g/l
ALP	540 iu/l
Bilirubin	67 $\mu$ mol/l
ALT	45 iu/l

What is the most likely diagnosis?

- ☐ A. Hepatic abscess
- ☐ B. Fungal obstruction of the bile duct
- ☐ C. Duodenal adenoma
- ☐ D. Primary biliary cirrhosis
- ☐ E. Sclerosing cholangitis

Next question

The LFTs clearly show a cholestatic picture. Given the background of HIV the most likely cause is sclerosing cholangitis

**HIV: biliary and pancreatic disease**

The most common cause of biliary disease in patients with HIV is sclerosing cholangitis due to infections such as CMV, Cryptosporidium and Microsporidia

Pancreatitis in the context of HIV infection may be secondary to anti-retroviral treatment (especially didanosine) or by opportunistic infections e.g. CMV

A 23-year-old nurse is reviewed in occupational health following a needle stick injury from a man known to be a carrier of hepatitis B. Which one of the following would appear first during acute hepatitis B infection?

- |                       |             |
|-----------------------|-------------|
| <input type="radio"/> | A. HBsAg    |
| <input type="radio"/> | B. HBeAg    |
| <input type="radio"/> | C. anti-HBc |
| <input type="radio"/> | D. anti-HBs |
| <input type="radio"/> | E. HBcAg    |

[Next question](#)

### Hepatitis B serology

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months. IgG anti-HBc persists
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

### Example results

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

A 31-year-old man with ulcerative colitis presents with a worsening of his symptoms. He is passing around four loose stools a day which do not contain blood. He has also experienced some urgency and tenesmus but is otherwise systemically well. What is the most appropriate management?

<input type="radio"/>	A. Rectal mesalazine
<input type="radio"/>	B. Oral metronidazole
<input type="radio"/>	C. Rectal corticosteroids
<input type="radio"/>	D. Observe with review in 7 days time
<input type="radio"/>	E. Oral loperamide

[Next question](#)

### Ulcerative colitis: management

Treatment can be divided into inducing and maintaining remission

Inducing remission

- treatment depends on the extent and severity of disease
- rectal aminosalicylates or steroids: for distal colitis rectal mesalazine has been shown to be superior to rectal steroids
- oral aminosalicylates or steroids
- severe colitis should be referred to hospital

Maintaining remission

- oral aminosalicylates e.g. Mesalazine
- azathioprine and mercaptopurine
- methotrexate is not recommended for the management of ulcerative colitis (in contrast to Crohn's disease)
- there is some evidence that probiotics may prevent relapse in patients with mild to moderate disease

**Question 37 of 151**

Next

A 65-year-old man with liver cirrhosis of unknown cause is reviewed in clinic. Which one of the following factors is most likely to indicate a poor prognosis?

- ☐ A. Alanine transaminase > 200 u/l
- ☐ B. Caput medusae
- ☐ C. Ascites
- ☐ D. Gynecomastia
- ☐ E. Splenomegaly

Next question

**Child-Pugh classification of liver cirrhosis**

The Child-Pugh classification is a scoring system to assess the severity of liver cirrhosis

Score	1	2	3
Bilirubin ( $\mu\text{mol/l}$ )	<34	34-50	>50
Albumin (g/l)	>35	28-35	<28
Prothrombin time, prolonged by (s)	<4	4-6	>6
Encephalopathy	none	mild	marked
Ascites	none	mild	marked

Summation of the scores allows the severity to be graded either A, B or C:

- < 7 = A
- 7-9 = B
- > 9 = C

**Question 38 of 151**

Next

A 25-year-old female currently under investigation for secondary amenorrhoea presents with jaundiced sclera. On examination spider naevi are present along with tender hepatomegaly. Blood tests show:

Hb	11.6 g/dl
Plt	$145 \times 10^9/l$
WCC	$6.4 \times 10^9/l$
Albumin	33 g/l
Bilirubin	78 $\mu\text{mol/l}$
ALT	245 iu/l

What is the most likely diagnosis?

<input type="radio"/>	A. Haemochromatosis
<input type="radio"/>	B. Wilson's disease
<input type="radio"/>	C. Primary biliary cirrhosis
<input type="radio"/>	D. Autoimmune hepatitis
<input type="radio"/>	E. Primary sclerosing cholangitis

Next question

The combination of deranged LFTs combined with secondary amenorrhoea in a young female strongly suggest autoimmune hepatitis

**Autoimmune hepatitis**

Autoimmune hepatitis is condition of unknown aetiology which is most commonly seen in young females. Recognised associations include other autoimmune disorders, hypergammaglobulinaemia and HLA B8, DR3. Three types of autoimmune hepatitis have been characterised according to the types of circulating antibodies present

Type I	Type II	Type III
Anti-nuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA)	Anti-liver/kidney microsomal type 1 antibodies (LKM1)	Soluble liver-kidney antigen
Affects both adults and children	Affects children only	Affects adults in middle-age

Features



- may present with signs of chronic liver disease
- acute hepatitis: fever, jaundice etc (only 25% present in this way)
- amenorrhoea (common)
- ANA/SMA/LKM1 antibodies, raised IgG levels
- liver biopsy: inflammation extending beyond limiting plate 'piecemeal necrosis', bridging necrosis

## Management

- steroids, other immunosuppressants e.g. azathioprine
- liver transplantation

Which of the following statements is true regarding the genetics of colon cancer?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Hereditary non-polyposis colorectal carcinoma is a autosomal recessive condition          |
| <input type="radio"/> | B. The adenomatous polyposis coli gene is located on chromosome 12                           |
| <input type="radio"/> | C. Around 50% of patients with familial adenomatous polyposis develop colon cancer           |
| <input type="radio"/> | D. Both hereditary and non-hereditary colon cancers typically present at 60-70 yrs of age    |
| <input type="radio"/> | E. Non-inherited colon cancer often involves mutation of the adenomatous polyposis coli gene |

Next question

### Colorectal cancer: genetics

It is currently thought there are three types of colon cancer:

- sporadic (95%)
- hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
- familial adenomatous polyposis (FAP, <1%)

Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene. It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC, an autosomal dominant condition, is the most common form of inherited colon cancer. Around 90% of patients develop cancers, often of the proximal colon, which are usually poorly differentiated and highly aggressive. Currently seven mutations have been identified, which affect genes involved in DNA mismatch repair leading to microsatellite instability. The most common genes involved are:

- MSH2 (60% of cases)
- MLH1 (30%)

The Amsterdam criteria are sometimes used to aid diagnosis:

- at least 3 family members with colon cancer
- the cases span at least two generations
- at least one case diagnosed before the age of 50 years

FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years. Patients inevitably develop carcinoma. It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5. Genetic testing can be done by analysing DNA from a patient's white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.

Patients with FAP are also at risk from duodenal tumours. A variant of FAP called Gardner's syndrome can also feature osteomas of the skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on the skin

You wish to screen a patient for hepatitis B infection. Which one of the following is the most suitable test to perform?

<input type="radio"/>	A. HBcAg
<input type="radio"/>	B. HBsAg
<input type="radio"/>	C. Hepatitis B viral load
<input type="radio"/>	D. anti-HBs
<input type="radio"/>	E. HBeAg

[Next question](#)

A positive anti-HBs would imply immunity through either previous immunisation or disease. A positive HBsAg implies either acute or chronic hepatitis B.

### Hepatitis B serology

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months. IgG anti-HBc persists
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

### Example results

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

**Question 41 of 151**

Next

A 54-year-old female with a history of scleroderma presents with chronic diarrhoea and bloating. Blood tests show a mild macrocytic anaemia. A diagnosis of small bowel bacterial overgrowth is suspected. Which one of the following tests is most likely to confirm the diagnosis?

<input type="radio"/>	A. Jejunal biopsy
<input type="radio"/>	B. Small bowel aspiration and culture
<input type="radio"/>	C. <sup>14</sup> C-xylose breath test
<input type="radio"/>	D. Small bowel meal
<input type="radio"/>	E. <sup>14</sup> C-glycocholate breath test

Next question

Whilst small bowel aspiration and culture is the gold standard investigation in this situation, its use is often limited due to resource limitations. Please see the British Society of Gastroenterology guidelines

The hydrogen breath test is another option. It has low sensitivity but high specificity

**Bacterial overgrowth: investigation**

The gold standard investigation of bacterial overgrowth is small bowel aspiration and culture

Other possible investigations include:

- hydrogen breath test
- <sup>14</sup>C-xylose breath test
- <sup>14</sup>C-glycocholate breath test: used increasingly less due to low specificity

In practice many clinicians give an empirical course of antibiotics as a trial

A 52-year-old woman is diagnosed with non-alcoholic steatohepatitis following a liver biopsy. What is the single most important step to help prevent the progression of her disease?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Stop smoking                 |
| <input type="radio"/> | B. Start statin therapy         |
| <input type="radio"/> | C. Eat more omega-3 fatty acids |
| <input type="radio"/> | D. Start sulfonylurea therapy   |
| <input type="radio"/> | E. Weight loss                  |

### Non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in the developed world. It is largely caused by obesity and describes a spectrum of disease ranging from:

- steatosis - fat in the liver
- steatohepatitis - fat with inflammation, non-alcoholic steatohepatitis (NASH), see below
- progressive disease may cause fibrosis and liver cirrhosis

NAFLD is thought to represent the hepatic manifestation of the metabolic syndrome and hence insulin resistance is thought to be the key mechanism leading to steatosis

Non-alcoholic steatohepatitis (NASH) is a term used to describe liver changes similar to those seen in alcoholic hepatitis in the absence of a history of alcohol abuse. It is relatively common and thought to affect around 3-4% of the general population. The progression of disease in patients with NASH may be responsible for a proportion of patients previously labelled as cryptogenic cirrhosis

#### Associated factors

- obesity
- hyperlipidaemia
- type 2 diabetes mellitus
- jejunoileal bypass
- sudden weight loss/starvation

#### Features

- usually asymptomatic
- hepatomegaly
- ALT is typically greater than AST
- increased echogenicity on ultrasound

## Management

- the mainstay of treatment is lifestyle changes (particularly weight loss) and monitoring
- there is ongoing research into the role of gastric banding and insulin-sensitising drugs (e.g. Metformin)

**Question 43 of 151**

Next

A 31-year-old female is admitted to the Emergency Department following a paracetamol overdose. The paracetamol level comes back as elevated but the doctor is unsure which treatment line to use. Which one of the following features in the medical history would classify the patient as high risk?

<input type="radio"/>	A. Hypothyroidism
<input type="radio"/>	B. Anorexia nervosa
<input type="radio"/>	C. Previous paracetamol overdose
<input type="radio"/>	D. Combined overdose with codeine
<input type="radio"/>	E. Long-term sodium valproate use

Next question

Paracetamol overdose - high risk if chronic alcohol, HIV, anorexia or P450 inducers

**Paracetamol overdose: risk factors**

The following groups of patients are at an increased risk of developing hepatotoxicity following a paracetamol overdose:

- patients taking liver enzyme-inducing drugs (rifampicin, phenytoin, carbamazepine, chronic alcohol excess, St John's Wort)
- malnourished patients (e.g. anorexia or bulimia, cystic fibrosis, hepatitis C, alcoholism, HIV)
- patients who have not eaten for a few days



A 26-year-old woman who is known to have type 1 diabetes mellitus presents with a three-month history of diarrhoea, fatigue and weight loss. She has tried excluding gluten from her diet for the past 4 weeks and feels much better. She requests to be tested so that a diagnosis of coeliac disease is confirmed. What is the most appropriate next step?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Check her HbA1c   |
| <input type="radio"/> | B. No need for further investigation as the clinical response is diagnostic  |
| <input type="radio"/> | C. Check anti-endomysial antibodies  |
| <input type="radio"/> | D. Arrange a jejunal biopsy  |
| <input type="radio"/> | E. Ask her to reintroduce gluten for the next 6 weeks before further testing |

Serological tests and jejunal biopsy may be negative if the patient is following a gluten-free diet. The patient should eat some gluten in more than one meal every day for at least 6 weeks before further testing.

### Coeliac disease: investigation

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis).

Diagnosis is made by a combination of immunology and jejunal biopsy. Villous atrophy and immunology normally reverses on a gluten-free diet.

NICE issued guidelines on the investigation of coeliac disease in 2009. If patients are already taking a gluten-free diet they should be asked, if possible, to reintroduce gluten for at least 6 weeks prior to testing.

#### Immunology

- tissue transglutaminase (TTG) antibodies (IgA) are first-choice according to NICE
- endomyseal antibody (IgA)
- anti-gliadin antibody (IgA or IgG) tests are not recommended by NICE
- anti-casein antibodies are also found in some patients

#### Jejunal biopsy

- villous atrophy
- crypt hyperplasia
- increase in intraepithelial lymphocytes
- lamina propria infiltration with lymphocytes

Rectal gluten challenge has been described but is not widely used

What is the most common cause of hepatocellular carcinoma in the United Kingdom?

<input type="radio"/>	A. Haemochromatosis
<input type="radio"/>	B. Hepatitis B
<input type="radio"/>	C. Alcohol excess
<input type="radio"/>	D. Aflatoxin
<input type="radio"/>	E. Hepatitis C

Next question

#### Hepatocellular carcinoma

- hepatitis B most common cause worldwide
- hepatitis C most common cause in Europe

### Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the third most common cause of cancer worldwide. Chronic hepatitis B is the most common cause of HCC worldwide with chronic hepatitis C being the most common cause in Europe.

The main risk factor for developing HCC is liver cirrhosis, for example secondary\* to hepatitis B & C, alcohol, haemochromatosis and primary biliary cirrhosis. Other risk factors include:

- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda
- male sex
- diabetes mellitus, metabolic syndrome

#### Features

- tends to present late
- features of liver cirrhosis or failure may be seen: jaundice, ascites, RUQ pain, hepatomegaly, pruritus, splenomegaly
- possible presentation is decompensation in a patient with chronic liver disease

Screening with ultrasound (+/- alpha-fetoprotein) should be considered for high risk groups such as:

- patients liver cirrhosis secondary to hepatitis B & C or haemochromatosis
- men with liver cirrhosis secondary to alcohol

Management options

- early disease: surgical resection
- liver transplantation
- radiofrequency ablation
- transarterial chemoembolisation
- sorafenib: a multikinase inhibitor

\*Wilson's disease is an exception

A patient presents with gastrointestinal symptoms. Which one of the following features in the history would be least consistent with making a diagnosis of irritable bowel syndrome?

<input type="radio"/>	A. Urgency to open bowels
<input type="radio"/>	B. Symptoms made worse by eating
<input type="radio"/>	C. 62-year-old female
<input type="radio"/>	D. Passage of mucous with stool
<input type="radio"/>	E. Bladder symptoms

Onset after 60 years of age is considered a red flag in the new NICE guidelines.

### Irritable bowel syndrome: diagnosis

NICE published clinical guidelines on the diagnosis and management of irritable bowel syndrome (IBS) in 2008

The diagnosis of IBS should be considered if the patient has had the following for at least 6 months:

- abdominal pain, and/or
- bloating, and/or
- change in bowel habit

A positive diagnosis of IBS should be made if the patient has abdominal pain relieved by defecation or associated with altered bowel frequency stool form, in addition to 2 of the following 4 symptoms:

- altered stool passage (straining, urgency, incomplete evacuation)
- abdominal bloating (more common in women than men), distension, tension or hardness
- symptoms made worse by eating
- passage of mucus

Features such as lethargy, nausea, backache and bladder symptoms may also support the diagnosis

Red flag features should be enquired about:

- rectal bleeding
- unexplained/unintentional weight loss
- family history of bowel or ovarian cancer
- onset after 60 years of age

Suggested primary care investigations are:

- full blood count
- ESR/CRP
- coeliac disease screen (tissue transglutaminase antibodies)

A 27-year-old woman with a history of depression presents to the Emergency Department. She reports taking 50 paracetamol tablets yesterday. Bloods are taken on admission. Which one of the following would most strongly indicate the need for a liver transplant?

<input type="radio"/>	A. Blood glucose 2.2 mmol/l
<input type="radio"/>	B. ALT 2364 iu/l
<input type="radio"/>	C. INR 4.1
<input type="radio"/>	D. Creatinine 230 $\mu$ mol/l
<input type="radio"/>	E. Arterial pH 7.27

[Next question](#)

The arterial pH is the single most important factor according to the King's College Hospital criteria for liver transplantation.

### Paracetamol overdose: management

#### Management

The following is based on the current BNF guidance. The National Poisons Information Service/TOXBASE should always be consulted for situations outside of the normal parameters.

Activated charcoal should be given if:

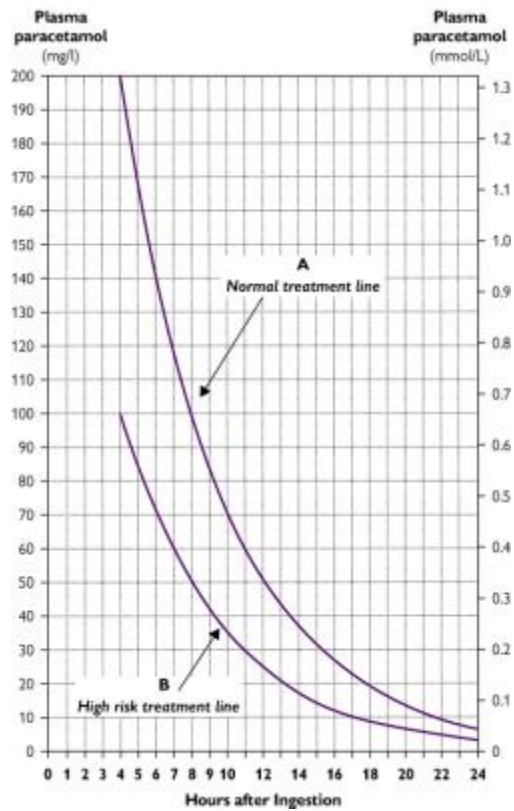
- paracetamol dose is in excess of 150 mg/kg (75 mg/kg if high-risk, see below) or 12 g, whichever is the smaller, and;
- the paracetamol was ingested in the previous hour

Patients presenting within 8 hours

- paracetamol levels (along with U&Es, LFTs and prothrombin time) should be checked 4 hours after ingestion (earlier samples may be misleading)
- the value should be plotted on a paracetamol treatment graph (see below)
- if the value is above the relevant treatment line intravenous acetylcysteine should be given

Patients presenting 8-24 hours after ingestion

- take an immediate blood sample for paracetamol levels, U&Es, LFTs and prothrombin time
- start acetylcysteine immediately if it is thought that more than 150 mg/kg body weight has been ingested. If the high risk (see below) consider treatment at a lower dose (75 mg/kg)
- otherwise wait for the paracetamol level, give intravenous acetylcysteine if the value is above the relevant treatment line



The following groups of patients are at an increased risk of developing hepatotoxicity following a paracetamol overdose and hence are considered 'high-risk':

- patients taking liver enzyme-inducing drugs (rifampicin, phenytoin, carbamazepine, chronic alcohol excess, St John's Wort)
- malnourished patients (e.g. anorexia or bulimia, cystic fibrosis, hepatitis C, alcoholism, HIV)
- patients who have not eaten for a few days

#### **King's College Hospital criteria for liver transplantation (paracetamol liver failure)**

Arterial pH < 7.3, 24 hours after ingestion

or all of the following:

- prothrombin time > 100 seconds
- creatinine > 300  $\mu\text{mol/l}$
- grade III or IV encephalopathy

A 64-year-old female with a history of COPD and hypertension presents with pain on swallowing. Current medication includes a salbutamol and becotide inhaler, bendrofluazide and amlodipine. What is the most likely cause of the presentation?

- ☐ A. Myasthenia gravis precipitated by bendrofluazide
- ☐ B. Oesophageal web
- ☐ C. Achalasia secondary to amlodipine
- ☐ D. Oesophageal candidiasis
- ☐ E. Oesophageal cancer

Pain on swallowing (odynophagia) is a typical of oesophageal candidiasis, a well documented complication of inhaled steroid therapy

### Dysphagia

The table below gives characteristic exam question features for conditions causing dysphagia:

<b>Oesophageal cancer</b>	Dysphagia may be associated with weight loss, anorexia or vomiting during eating Past history may include Barrett's oesophagus, GORD, excessive smoking or alcohol use
<b>Oesophagitis</b>	May be history of heartburn Odynophagia but no weight loss and systemically well
<b>Oesophageal candidiasis</b>	There may be a history of HIV or other risk factors such as steroid inhaler use
<b>Achalasia</b>	Dysphagia of both liquids and solids from the start Heartburn Regurgitation of food - may lead to cough, aspiration pneumonia etc
<b>Pharyngeal pouch</b>	More common in older men Represents a posteromedial herniation between thyropharyngeus and cricopharyngeus muscles Usually not seen but if large then a midline lump in the neck that gurgles on palpation Typical symptoms are dysphagia, regurgitation, aspiration and chronic cough. Halitosis may occasionally be seen
<b>Systemic sclerosis</b>	Other features of CREST syndrome may be present, namely Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia
<b>Myasthenia gravis</b>	Other symptoms may include extraocular muscle weakness or ptosis Dysphagia with liquids as well as solids
<b>Globus hystericus</b>	May be history of anxiety Symptoms are often intermittent

**Question 49 of 151**

According to recent NICE guidelines, which one of the following may have a role in the management of irritable bowel syndrome?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Reflexology  |
| <input type="radio"/> | B. Acupuncture  |
| <input type="radio"/> | C. Aloe vera    |
| <input type="radio"/> | D. Homeopathy   |
| <input type="radio"/> | E. Hypnotherapy |

[Next question](#)**Irritable bowel syndrome: management**

The management of irritable bowel syndrome (IBS) is often difficult and varies considerably between patients. NICE issued guidelines in 2008

First-line pharmacological treatment - according to predominant symptom

- pain: antispasmodic agents
- constipation: laxatives but avoid lactulose
- diarrhoea: loperamide is first-line

Second-line pharmacological treatment

- low-dose tricyclic antidepressants (e.g. amitriptyline 5-10 mg) are used in preference to selective serotonin reuptake inhibitors

Other management options

- psychological interventions - if symptoms do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile (refractory IBS), consider referring for cognitive behavioural therapy, hypnotherapy or psychological therapy
- complementary and alternative medicines: 'do not encourage use of acupuncture or reflexology for the treatment of IBS'



## General dietary advice

- have regular meals and take time to eat
- avoid missing meals or leaving long gaps between eating
- drink at least 8 cups of fluid per day, especially water or other non-caffeinated drinks such as herbal teas
- restrict tea and coffee to 3 cups per day
- reduce intake of alcohol and fizzy drinks
- consider limiting intake of high-fibre food (for example, wholemeal or high-fibre flour and breads, cereals high in bran, and whole grains such as brown rice)
- reduce intake of 'resistant starch' often found in processed foods
- limit fresh fruit to 3 portions per day
- for diarrhoea, avoid sorbitol
- for wind and bloating consider increasing intake of oats (for example, oat-based

breakfast cereal or porridge) and linseeds (up to one tablespoon per day).

Which one of the following investigations is considered the gold standard for the diagnosis of gastro-oesophageal reflux disease?

<input type="radio"/>	A. Endoscopy
<input checked="" type="radio"/>	B. 24hr oesophageal pH monitoring
<input type="radio"/>	C. Oesophageal manometry
<input type="radio"/>	D. Barium swallow
<input type="radio"/>	E. CT thorax

[Next question](#)

24hr oesophageal pH monitoring is gold standard investigation in GORD

## GORD: investigation

### Overview

- poor correlation between symptoms and endoscopy appearance

Indications for upper GI endoscopy:

- age > 55 years
- symptoms > 4 weeks or persistent symptoms despite treatment
- dysphagia
- relapsing symptoms
- weight loss

If endoscopy is negative consider 24-hr oesophageal pH monitoring (the gold standard test for diagnosis)

**Question 51 of 151**

Next

A 27-year-old man with multiple pigmented freckles on his lips and face is investigated for iron-deficiency anaemia. A diagnosis of Peutz-Jeghers syndrome is suspected. What is the mode of inheritance?

- |                                  |                              |
|----------------------------------|------------------------------|
| <input type="radio"/>            | A. Autosomal recessive       |
| <input type="radio"/>            | B. Mitochondrial inheritance |
| <input type="radio"/>            | C. X-linked dominant         |
| <input checked="" type="radio"/> | D. Autosomal dominant        |
| <input type="radio"/>            | E. X-linked recessive        |

Next question

Peutz-Jeghers syndrome - autosomal dominant

**Peutz-Jeghers syndrome**

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

**Genetics**

- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

**Features**

- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

**Management**

- conservative unless complications develop

The increased risk of oesophageal malignancy in patients with Barrett's oesophagus is approximately:

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. No increased risk      |
| <input type="radio"/> | B. Twice risk             |
| <input type="radio"/> | C. 5 times risk           |
| <input type="radio"/> | D. 50 - 100 times risk    |
| <input type="radio"/> | E. 500 - 1,000 times risk |

Next question

### Barrett's oesophagus

Barrett's refers to the metaplasia of the lower oesophageal mucosa, with the usual squamous epithelium being replaced by columnar epithelium. There is an increased risk of oesophageal adenocarcinoma, estimated at 50-100 fold.

#### Histological features

- the columnar epithelium may resemble that of either the cardiac region of the stomach or that of the small intestine (e.g. with goblet cells, brush border)

#### Management

- endoscopic surveillance with biopsies
- high-dose proton pump inhibitor

Where do the majority of VIPomas arise from?

<input type="radio"/>	A. Small intestine
<input type="radio"/>	B. Pituitary
<input type="radio"/>	C. Pancreas
<input type="radio"/>	D. Antrum of stomach
<input type="radio"/>	E. Pylorus of stomach

Next question

## VIPoma

VIP (vasoactive intestinal peptide)

- source: small intestine, pancreas
- stimulation: neural
- actions: stimulates secretion by pancreas and intestines, inhibits acid and pepsinogen secretion

VIPoma

- 90% arise from pancreas
- large volume diarrhoea
- weight loss
- dehydration
- hypokalaemia, hypochlorhydria

Which one of the following is not associated with oesophageal cancer?

<input type="radio"/>	A. Achalasia
<input type="radio"/>	B. Smoking
<input type="radio"/>	C. Gastro-oesophageal reflux disease
<input type="radio"/>	D. <i>Helicobacter pylori</i>
<input type="radio"/>	E. Alcohol

Next question

*Helicobacter pylori* may actually be protective against oesophageal cancer

### Oesophageal cancer

Until recent times oesophageal cancer was most commonly due to a squamous cell carcinoma but the incidence of adenocarcinoma is rising rapidly. Adenocarcinoma is now the most common type of oesophageal cancer and is more likely to develop in patients with a history of gastro-oesophageal reflux disease (GORD) or Barrett's.

The majority of tumours are in the middle third of the oesophagus.

#### Risk factors

- smoking
- alcohol
- GORD
- Barrett's oesophagus
- achalasia
- Plummer-Vinson syndrome
- rare: coeliac disease, scleroderma

A 45-year-old man is noted to have non-tender, smooth hepatomegaly associated Dupuytren's contracture and parotid enlargement. He recently returned from a holiday in Thailand. What is the likely diagnosis?

<input type="radio"/>	A. Primary hepatoma
<input type="radio"/>	B. Hydatid disease
<input type="radio"/>	C. Alcoholic liver disease
<input type="radio"/>	D. Viral hepatitis
<input type="radio"/>	E. Tricuspid regurgitation

[Next question](#)

Both Dupuytren's contracture and parotitis are associated with alcoholic liver disease. Whilst a history of alcohol excess would normally be volunteered it should be remembered many patients will lie about their alcohol intake.

The recent holiday in Thailand is a distractor.

### Hepatomegaly

Common causes of hepatomegaly

- Cirrhosis: if early disease, later liver decreases in size. Associated with a non-tender, firm liver
- Malignancy: metastatic spread or primary hepatoma. Associated with a hard, irregular. liver edge
- Right heart failure: firm, smooth, tender liver edge. May be pulsatile

Other causes

- viral hepatitis
- glandular fever
- malaria
- abscess: pyogenic, amoebic
- hydatid disease
- haematological malignancies
- haemochromatosis
- primary biliary cirrhosis
- sarcoidosis, amyloidosis

A 59-year-old female presents with a two month history of indigestion. She is otherwise well, has not had a similar episode before and takes no regular medication. Of note there is no recent weight loss or vomiting and abdominal examination is unremarkable. What is the most appropriate initial management?

<input type="radio"/>	A. Long-term course of a H2 receptor antagonist
<input type="radio"/>	B. Lifestyle advice with follow-up appointment in one month
<input type="radio"/>	C. Urgent referral for endoscopy
<input type="radio"/>	D. One month course of a full-dose proton pump inhibitor
<input type="radio"/>	E. Urea breath testing and treat for H pylori if positive

[Next question](#)

This patient meets the criteria for urgent referral for endoscopy as she is older than 55 years, has recent onset, persistent and unexplained symptoms

### Dyspepsia

In 2004 NICE published guidelines for the management of dyspepsia in primary care. These take into account the age of the patient (whether younger or older than 55 years) and the presence or absence of 'alarm signs':

- chronic gastrointestinal bleeding
- progressive unintentional weight loss
- progressive difficulty swallowing
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal

### Deciding whether urgent referral for endoscopy is needed

Urgent referral (within 2 weeks) is indicated for patients with any alarm signs irrespective of age

Routine endoscopic investigation of patients of any age, presenting with dyspepsia and without alarm signs is not necessary, however

Patients aged 55 years and over should be referred urgently for endoscopy if dyspepsia symptoms are:

- recent in onset rather than recurrent and
- unexplained (e.g. New symptoms which cannot be explained by precipitants such as NSAIDs) and
- persistent: continuing beyond a period that would normally be associated with self-limiting problems (e.g. Up to four to six weeks, depending on the severity of signs and symptoms)



## **Managing patients who do not meet referral criteria ('undiagnosed dyspepsia')**

This can be summarised at a step-wise approach

- 1. Review medications for possible causes of dyspepsia
- 2. Lifestyle advice
- 3. Trial of full-dose PPI for one month\*
- 4. 'Test and treat' using carbon-13 urea breath test

\*it is unclear from studies whether a trial of a PPI or a 'test and treat' should be used first

A 19-year-old man is referred to the general medical clinic. For the past six months his family have noted increasing behavioural and speech problems. He himself has noticed that he is more clumsy than normal and reports excessive salivation. His older brother died of liver disease. Given the likely underlying condition what is the most appropriate therapy?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Vitamin B6 supplements       |
| <input type="radio"/> | B. Venesection                  |
| <input type="radio"/> | C. Ribavirin + interferon alpha |
| <input type="radio"/> | D. Pulsed methylprednisolone    |
| <input type="radio"/> | E. Penicillamine                |

This man is likely to have Wilson's disease.

### Wilson's disease

Wilson's disease is an autosomal recessive disorder characterised by excessive copper deposition in the tissues. Metabolic abnormalities include increased copper absorption from the small intestine and decreased hepatic copper excretion. Wilson's disease is caused by a defect in the ATP7B gene located on chromosome 13

The onset of symptoms is usually between 10 - 25 years. Children usually present with liver disease whereas the first sign of disease in young adults is often neurological disease

Features result from excessive copper deposition in the tissues, especially the brain, liver and cornea:

- liver: hepatitis, cirrhosis
- neurological: speech and behavioural problems are often the first manifestations. Also: excessive salivation, tremor, chorea
- Kayser-Fleischer rings
- renal tubular acidosis (esp. Fanconi syndrome)
- haemolysis
- blue nails

### Diagnosis

- reduced serum caeruloplasmin
- increased 24hr urinary copper excretion

### Management

- penicillamine (chelates copper) has been the traditional first-line treatment
- trientine hydrochloride is an alternative chelating agent which may become first-line treatment in the future
- tetrathiomolybdate is a newer agent that is currently under investigation

Which one of the following statements is incorrect regarding Dubin-Johnson syndrome?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Runs a benign course   |
| <input type="radio"/> | B. Due to a defect in the canalicular multispecific organic anion transporter |
| <input type="radio"/> | C. Causes defective hepatic bilirubin excretion                               |
| <input type="radio"/> | D. It is an autosomal recessive disorder                                      |
| <input type="radio"/> | E. Results in an unconjugated hyperbilirubinaemia                             |

Next question

### Dubin-Johnson syndrome

Dubin-Johnson syndrome is a benign autosomal recessive disorder resulting in hyperbilirubinaemia (conjugated, therefore present in urine). It is due to a defect in the canalicular multispecific organic anion transporter (cMOAT) protein. This causes defective hepatic bilirubin excretion

A 30-year-old woman presents with a three month history of indigestion. There is no history of weight loss, anorexia, dysphagia, vomiting or change in bowel habit and abdominal examination is unremarkable. Which one of the following may decrease the accuracy of a  $^{13}\text{C}$ -urea breath test?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Use of Gaviscon around 10 days ago                  |
| <input type="radio"/> | B. Use of ranitidine stopping 4 weeks ago              |
| <input type="radio"/> | C. Course of amoxicillin stopping 3 weeks ago          |
| <input type="radio"/> | D. Use of lansoprazole stopping 6 weeks ago            |
| <input type="radio"/> | E. Current use of the combined oral contraceptive pill |

Next question

Urea breath test - no antibiotics in past 4 weeks, no antisecretory drugs (e.g. PPI) in past 2 weeks

### ***Helicobacter pylori*: tests**

#### Urea breath test

- patients consume a drink containing carbon isotope 13 ( $^{13}\text{C}$ ) enriched urea
- urea is broken down by *H. pylori* urease
- after 30 mins patient exhale into a glass tube
- mass spectrometry analysis calculates the amount of  $^{13}\text{C}$   $\text{CO}_2$
- should not be performed within 4 weeks of treatment with an antibacterial or within 2 weeks of an antisecretory drug (e.g. a proton pump inhibitor)
- sensitivity 95-98%, specificity 97-98%

#### Rapid urease test (e.g. CLO test)

- biopsy sample is mixed with urea and pH indicator
- colour change if *H. pylori* urease activity
- sensitivity 90-95%, specificity 95-98%

#### Serum antibody

- remains positive after eradication
- sensitivity 85%, specificity 80%

### Culture of gastric biopsy

- provide information on antibiotic sensitivity
- sensitivity 70%, specificity 100%

### Gastric biopsy

- histological evaluation alone, no culture
- sensitivity 95-99%, specificity 95-99%

### Stool antigen test

- sensitivity 90%, specificity 95%

A 40-year-old man is investigated for abnormal liver function tests. It is decided to perform a liver biopsy. Which one of the following is a contraindication to liver biopsy?

<input type="radio"/>	A. ALT of 2,212 iu/l
<input type="radio"/>	B. Aspirin therapy
<input type="radio"/>	C. Platelet count of $100 \times 10^9/l$
<input type="radio"/>	D. Body mass index of $33 \text{ kg/m}^2$
<input type="radio"/>	E. Bile duct dilatation

[Next question](#)

With modern techniques such as ERCP and MRI cholangiography the risks of liver biopsy when there is extra-hepatic biliary obstruction are rarely justified.

### Liver biopsy

Contraindications to percutaneous liver biopsy

- deranged clotting (e.g.  $\text{INR} > 1.4$ )
- low platelets (e.g.  $< 60 \times 10^9/l$ )
- anaemia
- bile duct obstruction
- hydatid cyst
- haemoangioma
- uncooperative patient
- ascites

Which one of the following is least likely to cause malabsorption?

<input type="radio"/>	A. Systemic sclerosis
<input type="radio"/>	B. Cystic fibrosis
<input type="radio"/>	C. Primary biliary cirrhosis
<input type="radio"/>	D. Whipple's disease
<input type="radio"/>	E. Haemochromatosis

## Malabsorption

Malabsorption is characterised by diarrhoea, steatorrhoea and weight loss. Causes may be broadly divided into intestinal (e.g. villous atrophy), pancreatic (deficiency of pancreatic enzyme production or secretion) and biliary (deficiency of bile-salts needed for emulsification of fats)

### Intestinal causes of malabsorption

- coeliac disease
- Crohn's disease
- tropical sprue
- Whipple's disease
- Giardiasis
- brush border enzyme deficiencies (e.g. lactase insufficiency)

### Pancreatic causes of malabsorption

- chronic pancreatitis
- cystic fibrosis
- pancreatic cancer

### Biliary causes of malabsorption

- biliary obstruction
- primary biliary cirrhosis

### Other causes

- bacterial overgrowth (e.g. systemic sclerosis, diverticulae, blind loop)
- short bowel syndrome
- lymphoma

**Question 62 of 151**

Next

A 42-year-old woman is investigated for lethargy and diarrhoea. Investigations reveal positive anti-endomysial antibodies. Each of the following food stuffs should be avoided, except:

<input type="radio"/>	A. Beer
<input type="radio"/>	B. Rye
<input type="radio"/>	C. Maize
<input type="radio"/>	D. Bread
<input type="radio"/>	E. Pasta

Next question

**Coeliac disease: management**

The management of coeliac disease involves a gluten-free diet. Gluten containing cereals include:

- wheat: bread, pasta, pastry
- barley\*: beer
- rye
- oats\*\*

Some notable foods which are gluten-free include:

- rice
- potatoes
- corn (maize)

\*whisky is made using malted barley. Proteins such as gluten are however removed during the distillation process making it safe to drink for patients with coeliac disease

\*\*some patients with coeliac disease appear able to tolerate oats



Which one of the following statements best describes the prevention and treatment of hepatitis C?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. No vaccine is available and treatment is only successful in around 10-15% of patients |
| <input type="radio"/> | B. No vaccine and no treatment is available  |
| <input type="radio"/> | C. A vaccine is available and treatment is successful in around 50% of patients          |
| <input type="radio"/> | D. A vaccine is available but no treatment has been shown to be effective                |
| <input type="radio"/> | E. No vaccine is available but treatment is successful in around 50% of patients         |

### Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

#### Transmission

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

#### Features

- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

#### Complications

- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

#### Management of chronic infection

- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains
- the aim of treatment is sustained virological response (SVR), defined as undetectable

serum HCV RNA six months after the end of therapy

## Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

The most common type of inherited colorectal cancer:

<input type="radio"/>	A. Familial adenomatous polyposis
<input type="radio"/>	B. Li-Fraumeni syndrome
<input type="radio"/>	C. Hereditary non-polyposis colorectal carcinoma
<input type="radio"/>	D. Fanconi syndrome
<input type="radio"/>	E. Peutz-Jeghers syndrome

### Colorectal cancer: genetics

It is currently thought there are three types of colon cancer:

- sporadic (95%)
- hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
- familial adenomatous polyposis (FAP, <1%)

Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene. It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC, an autosomal dominant condition, is the most common form of inherited colon cancer. Around 90% of patients develop cancers, often of the proximal colon, which are usually poorly differentiated and highly aggressive. Currently seven mutations have been identified, which affect genes involved in DNA mismatch repair leading to microsatellite instability. The most common genes involved are:

- MSH2 (60% of cases)
- MLH1 (30%)

The Amsterdam criteria are sometimes used to aid diagnosis:

- at least 3 family members with colon cancer
- the cases span at least two generations
- at least one case diagnosed before the age of 50 years

FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years. Patients inevitably develop carcinoma. It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5. Genetic testing can be done by analysing DNA from a patient's white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.

Patients with FAP are also at risk from duodenal tumours. A variant of FAP called Gardner's syndrome can also feature osteomas of the skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on the skin

Which one of the following statements regarding hepatitis C is correct?

<input type="radio"/>	A. Cannot be transmitted vertically from mother to child
<input type="radio"/>	B. Interferon-alpha and ribavirin are the treatments of choice
<input type="radio"/>	C. It is more infectious than hepatitis B following a needle stick injury
<input type="radio"/>	D. Breast feeding is contraindicated in mothers with hepatitis C
<input type="radio"/>	E. HCV RNA is the initial investigation of choice for at-risk groups

Next question

## Hepatitis C

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### Features

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### Complications

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- hepatocellular cancer
- cryoglobulinaemia

### Management of chronic infection

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- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains
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serum HCV RNA six months after the end of therapy

#### Complications of treatment

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- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

**Question 66 of 151**

Next

A 17-year-old girl presents with a 6 week history of nausea and abdominal discomfort. Routine blood tests reveal the following.

Hb	10.9 g/dl
WBC	6.7 *10 <sup>9</sup> /l
Platelets	346 *10 <sup>9</sup> /l
Calcium	2.33 mmol/l
Bilirubin	7 µmol/l
ALP	262 u/l
ALT	35 u/l

What is the most likely diagnosis?

<input type="radio"/>	A. Alcoholic liver disease
<input type="radio"/>	B. Cholangiocarcinoma
<input type="radio"/>	C. Pregnancy
<input type="radio"/>	D. Gallstones
<input type="radio"/>	E. Primary biliary cirrhosis

Alkaline phosphatase is significantly elevated in pregnancy. This would also explain the borderline anaemia

**Alkaline phosphatase**

Causes of raised alkaline phosphatase (ALP)

- liver: cholestasis, hepatitis, fatty liver, neoplasia
- Paget's
- osteomalacia
- bone metastases
- hyperparathyroidism
- renal failure
- physiological: pregnancy, growing children, healing fractures

The table below splits the causes according to the calcium level

<b>Raised ALP and raised calcium</b>	<b>Raised ALP and low calcium</b>
<ul style="list-style-type: none"><li>• Bone metastases</li><li>• Hyperparathyroidism</li></ul>	<ul style="list-style-type: none"><li>• Osteomalacia</li><li>• Renal failure</li></ul>

A 36-year-old man is reviewed in clinic. He has recently been started on mesalazine 400mg tds for ulcerative colitis. Which one of the following adverse effects is least likely to be attributable to mesalazine?

<input type="radio"/>	A. Interstitial nephritis
<input type="radio"/>	B. Headaches
<input type="radio"/>	C. Acute pancreatitis
<input type="radio"/>	D. Agranulocytosis
<input type="radio"/>	E. Infertility

[Next question](#)

Oligospermia is seen in patients taking sulphasalazine due to the sulphapyridine moiety, which is not present in mesalazine

### Aminosalicylate drugs

5-aminosalicylic acid (5-ASA) is released in the colon and is not absorbed. It acts locally as an anti-inflammatory. The mechanism of action is not fully understood but 5-ASA may inhibit prostaglandin synthesis

#### Sulphasalazine

- a combination of sulphapyridine (a sulphonamide) and 5-ASA
- many side-effects are due to the sulphapyridine moiety: rashes, oligospermia, headache, Heinz body anaemia
- other side-effects are common to 5-ASA drugs (see mesalazine)

#### Mesalazine

- a delayed release form of 5-ASA
- sulphapyridine side-effects seen in patients taking sulphasalazine are avoided
- mesalazine is still however associated with side-effects such as GI upset, headache, agranulocytosis, pancreatitis\*, interstitial nephritis

#### Olsalazine

- two molecules of 5-ASA linked by a diazo bond, which is broken by colonic bacteria

\*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

**Question 68 of 151**

Next

A 45-year-old man is admitted to the Emergency Department with severe abdominal pain. He smokes 20 cigarettes a day and drinks approximately 50 units of alcohol per week. He also complains of sudden deterioration in vision. Fundoscopy reveals shows multiple micro infarcts (cotton wool spots). Which investigation would best confirm the most likely diagnosis?

<input type="radio"/>	A. Gastroscopy
<input type="radio"/>	B. Serum glucose
<input type="radio"/>	C. Amylase
<input type="radio"/>	D. Biliary USS
<input type="radio"/>	E. ECG

Next question

The cotton wool spots seen on fundoscopy represents Purtscher retinopathy. This condition may be seen following head trauma and in conditions such as acute pancreatitis, fat embolisation, amniotic fluid embolisation, and vasculitic diseases

**Acute pancreatitis: features**

Rare features associated with pancreatitis include:

- ischaemic (Purtscher) retinopathy - may cause temporary or permanent blindness



A 27-year-old female is referred to the medical outpatient clinic due to a long history of fatigue and joint pains. An autoimmune screen is done which is positive for smooth muscle antibodies. What is the most appropriate next investigation?

- ☐ A. Liver function tests
- ☐ B. Thyroid function tests
- ☐ C. Creatine kinase
- ☐ D. Serum glucose
- ☐ E. Electrocardiogram

Next question

Smooth muscle antibodies are associated with autoimmune hepatitis. Presentation is usually insidious and extrahepatic clinical features are common

### Autoimmune hepatitis

Autoimmune hepatitis is condition of unknown aetiology which is most commonly seen in young females. Recognised associations include other autoimmune disorders, hypergammaglobulinaemia and HLA B8, DR3. Three types of autoimmune hepatitis have been characterised according to the types of circulating antibodies present

Type I	Type II	Type III
Anti-nuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA)	Anti-liver/kidney microsomal type 1 antibodies (LKM1)	Soluble liver-kidney antigen
Affects both adults and children	Affects children only	Affects adults in middle-age

### Features

- may present with signs of chronic liver disease
- acute hepatitis: fever, jaundice etc (only 25% present in this way)
- amenorrhoea (common)
- ANA/SMA/LKM1 antibodies, raised IgG levels
- liver biopsy: inflammation extending beyond limiting plate 'piecemeal necrosis', bridging necrosis

### Management

- steroids, other immunosuppressants e.g. azathioprine
- liver transplantation

Which one of the following conditions is least likely to develop following hepatitis B infection?

- ☐ A. Glomerulonephritis
- ☐ B. Hepatocellular carcinoma
- ☐ C. Acute pancreatitis
- ☐ D. Chronic infection
- ☐ E. Polyarteritis nodosa

Next question

Deterioration in patient with hepatitis B - ? hepatocellular carcinoma

## Hepatitis B

Hepatitis B is a double-stranded DNA virus and is spread through exposure to infected blood or body fluids, including vertical transmission from mother to child. The incubation period is 6-20 weeks.

Immunisation against hepatitis B (please see the Greenbook link for more details)

- contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology
- most schedules give 3 doses of the vaccine with a recommendation for a one-off booster 5 years following the initial primary vaccination
- at risk groups who should be vaccinated include: healthcare workers, intravenous drug users, sex workers, close family contacts of an individual with hepatitis B, individuals receiving blood transfusions regularly, chronic kidney disease patients who may soon require renal replacement therapy, prisoners, chronic liver disease patients
- around 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine. Risk factors include age over 40 years, obesity, smoking, alcohol excess and immunosuppression
- testing for anti-HBs is only recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease. In these patients anti-HBs levels should be checked 1-4 months after primary immunisation
- the table below shows how to interpret anti-HBs levels:

Anti-HBs level (mIU/ml)	Response
> 100	Indicates adequate response, no further testing required. Should still receive booster at 5 years

10 - 100	Suboptimal response - one additional vaccine dose should be given. If immunocompetent no further testing is required
< 10	Non-responder. Test for current or past infection. Give further vaccine course (i.e. 3 doses again) with testing following. If still fails to respond then HBIG would be required for protection if exposed to the virus

### Complications of hepatitis B infection

- chronic hepatitis (5-10%)
- fulminant liver failure (1%)
- hepatocellular carcinoma
- glomerulonephritis
- polyarteritis nodosa
- cryoglobulinaemia

### Management of hepatitis B

- pegylated interferon-alpha used to be the only treatment available. It reduces viral replication in up to 30% of chronic carriers. A better response is predicted by being female, < 50 years old, low HBV DNA levels, non-Asian, HIV negative, high degree of inflammation on liver biopsy
- however due to the side-effects of pegylated interferon it is now used less commonly in clinical practice. Oral antiviral medication is increasingly used with an aim to suppress viral replication (not in dissimilar way to treating HIV patients)
- examples include lamivudine, tenofovir and entecavir

Which one of the following is not associated with villous atrophy on jejunal biopsy?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Tropical sprue               |
| <input type="radio"/> | B. Coeliac disease              |
| <input type="radio"/> | C. Hypogammaglobulinaemia       |
| <input type="radio"/> | D. Familial Mediterranean Fever |
| <input type="radio"/> | E. Whipple's disease            |

[Next question](#)

Causes of villous atrophy (other than coeliacs): tropical sprue, Whipple's, lymphoma, hypogammaglobulinaemia

### Jejunal villous atrophy

Whilst coeliac disease is the classic cause of jejunal villous atrophy there are a number of other causes you need to be aware of

#### Causes

- coeliac disease
- tropical sprue
- hypogammaglobulinaemia
- gastrointestinal lymphoma
- Whipple's disease
- cow's milk intolerance

**Question 72 of 151**

Next

A 34-year-old male is admitted with central abdominal pain radiating through to the back and vomiting. The following results are obtained:

Amylase	1,245 u/dl
---------	------------

Which one of the following medications is most likely to be responsible?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Phenytoin        |
| <input type="radio"/> | B. Sodium valproate |
| <input type="radio"/> | C. Metoclopramide   |
| <input type="radio"/> | D. Sumatriptan      |
| <input type="radio"/> | E. Pizotifen        |

Next question

Sodium valproate induced pancreatitis is more common in young adults and tends to occur within the first few months of treatment. Asymptomatic elevation of the amylase level is seen in up to 10% of patients

**Acute pancreatitis: causes**

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RCP
- **D**rugs (azathioprine, mesalazine\*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

\*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

A 59-year-old woman presents with dysphagia. There is no history of heartburn, weight loss or change in bowel habit. During endoscopy there is some difficulty passing through the lower oesophageal sphincter but no other abnormality is noted. Which one of the following tests is most likely to reveal the diagnosis?

<input type="radio"/>	A. Oesophageal biopsy
<input type="radio"/>	B. Oesophageal manometry
<input type="radio"/>	C. Plain chest x-ray
<input type="radio"/>	D. Endoscopy ultrasound
<input type="radio"/>	E. CT thorax

[Next question](#)

The gold standard test for achalasia is oesophageal manometry

## Achalasia

Failure of oesophageal peristalsis and of relaxation of lower oesophageal sphincter (LOS) due to degenerative loss of ganglia from Auerbach's plexus i.e. LOS contracted, oesophagus above dilated. Achalasia typically presents in middle-age and is equally common in men and women.

### Clinical features

- dysphagia of BOTH liquids and solids
- typically variation in severity of symptoms
- heartburn
- regurgitation of food - may lead to cough, aspiration pneumonia etc
- malignant change in small number of patients

### Investigations

- manometry: excessive LOS tone which doesn't relax on swallowing - considered most important diagnostic test
- barium swallow shows grossly expanded oesophagus, fluid level
- CXR: wide mediastinum, fluid level

### Treatment

- intra-sphincteric injection of botulinum toxin
- Heller cardiomyotomy
- balloon dilation
- drug therapy has a role but is limited by side-effects

Which of the following is not a recognised complication of coeliac disease?

<input type="radio"/>	A. Hypersplenism
<input type="radio"/>	B. Osteoporosis
<input type="radio"/>	C. Lactose intolerance
<input type="radio"/>	D. Oesophageal cancer
<input type="radio"/>	E. Subfertility

Hypo-, not hypersplenism is seen in coeliac disease

### Coeliac disease

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis). It is strongly associated with HLA-DQ2 (95% of patients) and HLA-B8 (80%) as well as HLA-DR3 and HLA-DR7

In 2009 NICE issued guidelines on the investigation of coeliac disease. They suggest that the following patients should be screened for coeliac disease:

Signs and symptoms	Conditions
<ul style="list-style-type: none"> <li>Chronic or intermittent diarrhoea</li> <li>Failure to thrive or faltering growth (in children)</li> <li>Persistent or unexplained gastrointestinal symptoms including nausea and vomiting</li> <li>Prolonged fatigue ('tired all the time')</li> <li>Recurrent abdominal pain, cramping or distension</li> <li>Sudden or unexpected weight loss</li> <li>Unexplained iron-deficiency anaemia, or other unspecified anaemia</li> </ul>	<ul style="list-style-type: none"> <li>Autoimmune thyroid disease</li> <li>Dermatitis herpetiformis</li> <li>Irritable bowel syndrome</li> <li>Type 1 diabetes</li> <li>First-degree relatives (parents, siblings or children) with coeliac disease</li> </ul>

### Complications

- anaemia: iron, folate and vitamin B12 deficiency (folate deficiency is more common than vitamin B12 deficiency in coeliac disease)
- hyposplenism
- osteoporosis
- lactose intolerance
- enteropathy-associated T-cell lymphoma of small intestine
- subfertility, unfavourable pregnancy outcomes
- rare: oesophageal cancer, other malignancies

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Next

A 43-year-old man with type 2 diabetes mellitus presents with lethargy. His current medications include metformin and gliclazide, although the gliclazide may soon be stopped due to his obesity. A number of blood tests are ordered which reveal the following:

HbA1c	8.2%
Ferritin	204 ng/ml

Bilirubin	23 $\mu$ mol/l
ALP	162 u/l
ALT	120 u/l
AST	109 u/l

On discussing these results he states that he does not drink alcohol. What is the most likely cause of these abnormal results?

- ☐ A. Metformin-induced steatohepatitis
- ☐ B. Haemochromatosis
- ☐ C. Acute hepatitis secondary to gliclazide
- ☐ D. Cryptogenic cirrhosis
- ☐ E. Non-alcoholic fatty liver disease

Next question

Obese T2DM with abnormal LFTs - ? non-alcoholic fatty liver disease

By far the most likely diagnosis in an obese type 2 diabetic is non-alcoholic fatty liver disease. This patient will require a liver screen, ultrasound and liver biopsy to confirm the diagnosis.

A normal ferritin makes a diagnosis of haemochromatosis unlikely, although it should always be considered in patients with both abnormal LFTs and diabetes.

**Non-alcoholic fatty liver disease**

Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in the developed world. It is largely caused by obesity and describes a spectrum of disease ranging from:

- steatosis - fat in the liver
- steatohepatitis - fat with inflammation, non-alcoholic steatohepatitis (NASH), see below
- progressive disease may cause fibrosis and liver cirrhosis



NAFLD is thought to represent the hepatic manifestation of the metabolic syndrome and hence insulin resistance is thought to be the key mechanism leading to steatosis

Non-alcoholic steatohepatitis (NASH) is a term used to describe liver changes similar to those seen in alcoholic hepatitis in the absence of a history of alcohol abuse. It is relatively common and thought to affect around 3-4% of the general population. The progression of disease in patients with NASH may be responsible for a proportion of patients previously labelled as cryptogenic cirrhosis

#### Associated factors

- obesity
- hyperlipidaemia
- type 2 diabetes mellitus
- jejunoileal bypass
- sudden weight loss/starvation

#### Features

- usually asymptomatic
- hepatomegaly
- ALT is typically greater than AST
- increased echogenicity on ultrasound

#### Management

- the mainstay of treatment is lifestyle changes (particularly weight loss) and monitoring
- there is ongoing research into the role of gastric banding and insulin-sensitising drugs (e.g. Metformin)

A 45-year-old man with a history of alcohol excess is diagnosed as having grade 3 oesophageal varices during an outpatient endoscopy. Of the following options, what is the most appropriate management to prevent variceal bleeding?

<input type="radio"/>	A. Propranolol
<input type="radio"/>	B. Isosorbide mononitrate
<input type="radio"/>	C. Endoscopic sclerotherapy
<input type="radio"/>	D. Terlipressin
<input type="radio"/>	E. Lansoprazole

[Next question](#)

Endoscopic sclerotherapy now has little role in the prophylaxis of variceal haemorrhage.

### Oesophageal varices

#### Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent and is supported by NICE guidelines. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy. NICE recommend band ligation
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

#### Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

A 78-year-old woman is admitted with a productive cough and pyrexia to hospital. Chest x-ray shows a pneumonia and she is commenced on intravenous ceftriaxone. Four days following admission a stool sample is sent because of diarrhoea. This confirms the suspected diagnosis of *Clostridium difficile* diarrhoea and a 10-day course of oral metronidazole is started. After 10 days her diarrhoea is ongoing but she remains clinically stable. What is the most appropriate treatment?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Oral vancomycin for 14 days             |
| <input type="radio"/> | B. IV vancomycin for 3 days                |
| <input type="radio"/> | C. Oral rifampicin for 7 days              |
| <input type="radio"/> | D. Oral clindamycin for 7 days             |
| <input type="radio"/> | E. Oral metronidazole for a further 7 days |

[Next question](#)

The Health Protection Agency suggests switching to oral vancomycin in this scenario.

### ***Clostridium difficile***

*Clostridium difficile* is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading cause of *Clostridium difficile*.

#### Features

- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

#### Management

- first-line therapy is oral metronidazole for 10-14 days
- if severe or not responding to metronidazole then oral vancomycin may be used
- for life-threatening infections a combination of oral vancomycin and intravenous metronidazole should be used

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Next

A 25-year-old man presents with bloody diarrhoea associated with systemic upset. Blood tests show the following:

Hb	13.4 g/dl
Platelets	$467 \times 10^9/l$
WBC	$8.2 \times 10^9/l$
CRP	89 mg/l

A diagnosis of ulcerative colitis is suspected. Which part of the bowel is most likely to be affected?

- ☐ A. Sigmoid colon
- ☒ B. Rectum
- ☐ C. Ascending colon
- ☐ D. Descending colon
- ☐ E. Terminal ileum

Next question

Ulcerative colitis - the rectum is the most common site affected

**Ulcerative colitis**

Ulcerative colitis (UC) is a form of inflammatory bowel disease. Inflammation always starts at rectum (hence it is the most common site for UC), never spreads beyond ileocaecal valve and is continuous. The peak incidence of ulcerative colitis is in people aged 15-25 years and in those aged 55-65 years.

The initial presentation is usually following insidious and intermittent symptoms. Features include:

- bloody diarrhoea
- urgency
- tenesmus
- abdominal pain, particularly in the left lower quadrant
- extra-intestinal features (see below)

Questions regarding the 'extra-intestinal' features of inflammatory bowel disease are common:

	<b>Common to both Crohn's disease (CD) and Ulcerative colitis (UC)</b>	<b>Notes</b>
<b>Related to disease activity</b>	Arthritis: pauciarticular, asymmetric Erythema nodosum Episcleritis Osteoporosis	Arthritis is the most common extra-intestinal feature in both CD and UC Episcleritis is more common in CD
<b>Unrelated to disease activity</b>	Arthritis: polyarticular, symmetric Uveitis Pyoderma gangrenosum Clubbing Primary sclerosing cholangitis	Primary sclerosing cholangitis is much more common in UC Uveitis is more common in UC

## Pathology

- red, raw mucosa, bleeds easily
- no inflammation beyond submucosa (unless fulminant disease)
- widespread ulceration with preservation of adjacent mucosa which has the appearance of polyps ('pseudopolyps')
- inflammatory cell infiltrate in lamina propria
- neutrophils migrate through the walls of glands to form crypt abscesses
- depletion of goblet cells and mucin from gland epithelium
- granulomas are infrequent

## Barium enema

- loss of haustrations
- superficial ulceration, 'pseudopolyps'
- long standing disease: colon is narrow and short -'drainpipe colon'

A 31-year-old woman presents with symptoms consistent with coeliac disease. Which one of the following tests should be used first-line when screening patients for coeliac disease?

<input type="radio"/>	A. Anti-casein antibodies
<input type="radio"/>	B. Tissue transglutaminase antibodies
<input type="radio"/>	C. Anti-gliadin antibodies
<input type="radio"/>	D. Xylose absorption test
<input type="radio"/>	E. Anti-endomyseal antibodies

[Next question](#)

Coeliac disease - tissue transglutaminase antibodies first-line test

Tissue transglutaminase antibodies are recommended as the first-line serological test according to NICE.

### Coeliac disease: investigation

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis).

Diagnosis is made by a combination of immunology and jejunal biopsy. Villous atrophy and immunology normally reverses on a gluten-free diet.

NICE issued guidelines on the investigation of coeliac disease in 2009. If patients are already taking a gluten-free diet they should be asked, if possible, to reintroduce gluten for at least 6 weeks prior to testing.

#### Immunology

- tissue transglutaminase (TTG) antibodies (IgA) are first-choice according to NICE
- endomyseal antibody (IgA)
- anti-gliadin antibody (IgA or IgG) tests are not recommended by NICE
- anti-casein antibodies are also found in some patients

#### Jejunal biopsy

- villous atrophy
- crypt hyperplasia
- increase in intraepithelial lymphocytes
- lamina propria infiltration with lymphocytes

Rectal gluten challenge has been described but is not widely used

Which one the following disorders is most strongly associated with primary biliary cirrhosis?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Systemic sclerosis           |
| <input type="radio"/> | B. Thyroid disease              |
| <input type="radio"/> | C. Sjogren's syndrome           |
| <input type="radio"/> | D. Rheumatoid arthritis         |
| <input type="radio"/> | E. Systemic lupus erythematosus |

Next question

All of the above conditions are associated with primary biliary cirrhosis but Sjogren's syndrome is the most common, being seen in up to 80% of patients

### Primary biliary cirrhosis

Primary biliary cirrhosis is a chronic liver disorder typically seen in middle-aged females (female:male ratio of 9:1). The aetiology is not fully understood although it is thought to be an autoimmune condition. Interlobular bile ducts become damaged by a chronic inflammatory process causing progressive cholestasis which may eventually progress to cirrhosis. The classic presentation is itching in a middle-aged woman

#### Associations

- Sjogren's syndrome (seen in up to 80% of patients)
- rheumatoid arthritis
- systemic sclerosis
- thyroid disease

#### Diagnosis

- anti-mitochondrial antibodies (AMA) M2 subtype are present in 98% of patients and are highly specific
- smooth muscle antibodies in 30% of patients
- raised serum IgM

#### Management

- pruritus: cholestyramine
- fat-soluble vitamin supplementation
- ursodeoxycholic acid
- liver transplantation e.g. if bilirubin > 100 (PBC is a major indication) - recurrence in graft can occur but is not usually a problem

A 54-year-old female is diagnosed with primary biliary cirrhosis. What is her increased risk of developing hepatocellular cancer, compared to a standard population?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. 50% increased risk     |
| <input type="radio"/> | B. 3-fold increased risk  |
| <input type="radio"/> | C. 5-fold increased risk  |
| <input type="radio"/> | D. 10-fold increased risk |
| <input type="radio"/> | E. 20-fold increased risk |

[Next question](#)

### Primary biliary cirrhosis: features

Primary biliary cirrhosis is chronic liver disorder typically seen in middle-aged females (female:male ratio of 9:1). The aetiology is not fully understood although it is thought to be an autoimmune condition. Interlobular bile ducts become damaged by a chronic inflammatory process causing progressive cholestasis, which may eventually progress to cirrhosis. The classic presentation is itching in a middle-aged woman

#### Clinical features

- early: may be asymptomatic (e.g. raised ALP on routine LFTs) or fatigue, pruritus
- cholestatic jaundice
- hyperpigmentation, especially over pressure points
- xanthelasmas, xanthomata
- also: clubbing, hepatosplenomegaly
- late: may progress to liver failure

#### Complications

- malabsorption: osteomalacia, coagulopathy
- sicca syndrome occurs in 70% of cases
- portal hypertension: ascites, variceal haemorrhage
- hepatocellular cancer (20-fold increased risk)



A 71-year-old man presents with two year history of intermittent problems with swallowing. His wife has also noticed he has halitosis and is coughing at night. He has a past medical history of type 2 diabetes mellitus but states he is otherwise well. Of note his weight is stable and he has a good appetite. Clinical examination is unremarkable. What is the most likely diagnosis?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Oesophageal cancer           |
| <input type="radio"/> | B. Hiatus hernia                |
| <input type="radio"/> | C. Pharyngeal pouch             |
| <input type="radio"/> | D. Oesophageal candidiasis      |
| <input type="radio"/> | E. Benign oesophageal stricture |

[Next question](#)

Given the two year history and good health oesophageal cancer is much less likely

### Pharyngeal pouch

A pharyngeal pouch is a posteromedial diverticulum through Killian's dehiscence. Killian's dehiscence is a triangular area in the wall of the pharynx between the thyropharyngeus and cricopharyngeus muscles. It is more common in older patients and is 5 times more common in men

#### Features

- dysphagia
- regurgitation
- aspiration
- neck swelling which gurgles on palpation
- halitosis

A 27-year-old woman with chronic left iliac fossa pain and alternating bowel habit is diagnosed with irritable bowel syndrome. Initial treatment is tried with a combination of antispasmodics, laxatives and anti-motility agents. Unfortunately after 6 months there has been no significant improvement in her symptoms. According to recent NICE guidelines, what is the most appropriate next step?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Low-dose tricyclic antidepressant      |
| <input type="radio"/> | B. Cognitive behavioural therapy          |
| <input type="radio"/> | C. Refer for sigmoidoscopy                |
| <input type="radio"/> | D. Trial of probiotics                    |
| <input type="radio"/> | E. Selective serotonin reuptake inhibitor |

[Next question](#)

NICE recommend considering psychological interventions after 12 months. Tricyclic antidepressants should be used in preference to selective serotonin reuptake inhibitors

### Irritable bowel syndrome: management

The management of irritable bowel syndrome (IBS) is often difficult and varies considerably between patients. NICE issued guidelines in 2008

First-line pharmacological treatment - according to predominant symptom

- pain: antispasmodic agents
- constipation: laxatives but avoid lactulose
- diarrhoea: loperamide is first-line

Second-line pharmacological treatment

- low-dose tricyclic antidepressants (e.g. amitriptyline 5-10 mg) are used in preference to selective serotonin reuptake inhibitors

Other management options

- psychological interventions - if symptoms do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile (refractory IBS), consider referring for cognitive behavioural therapy, hypnotherapy or psychological therapy
- complementary and alternative medicines: 'do not encourage use of acupuncture or reflexology for the treatment of IBS'

## General dietary advice

- have regular meals and take time to eat
- avoid missing meals or leaving long gaps between eating
- drink at least 8 cups of fluid per day, especially water or other non-caffeinated drinks such as herbal teas
- restrict tea and coffee to 3 cups per day
- reduce intake of alcohol and fizzy drinks
- consider limiting intake of high-fibre food (for example, wholemeal or high-fibre flour and breads, cereals high in bran, and whole grains such as brown rice)
- reduce intake of 'resistant starch' often found in processed foods
- limit fresh fruit to 3 portions per day
- for diarrhoea, avoid sorbitol
- for wind and bloating consider increasing intake of oats (for example, oat-based

breakfast cereal or porridge) and linseeds (up to one tablespoon per day).

A 29-year-old man presents with a nine day history of watery diarrhoea that developed one week after returning from India. He had travelled around northern India for two months. On examination he is afebrile and his abdomen is soft and non-tender. What is the most likely causative organism?

- ☐ A. Amoebiasis
- ☐ B. Giardiasis
- ☐ C. *Campylobacter*
- ☐ D. *Shigella*
- ☐ E. *Salmonella*

[Next question](#)

The incubation period and prolonged, non-bloody diarrhoea point towards giardiasis

### Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one or more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

### Stereotypical histories

<b><i>Escherichia coli</i></b>	Common amongst travellers Watery stools Abdominal cramps and nausea
<b>Giardiasis</b>	Prolonged, non-bloody diarrhoea
<b>Cholera</b>	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
<b><i>Shigella</i></b>	Bloody diarrhoea Vomiting and abdominal pain
<b><i>Staphylococcus aureus</i></b>	Severe vomiting Short incubation period
<b><i>Campylobacter</i></b>	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be

	bloody  Complications include Guillain-Barre syndrome
<b><i>Bacillus cereus</i></b>	Two types of illness are seen <ul style="list-style-type: none"> <li>• vomiting within 6 hours, stereotypically due to rice</li> <li>• diarrhoeal illness occurring after 6 hours</li> </ul>
<b>Amoebiasis</b>	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

#### Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus*\*
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

\*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

Which one of the following is least useful in assessing the severity of a patient with liver cirrhosis?

- ☐ A. ALT
- ☐ B. Prothrombin time
- ☐ C. Bilirubin
- ☐ D. The presence of ascites
- ☐ E. The presence of encephalopathy

Next question

### Child-Pugh classification of liver cirrhosis

The Child-Pugh classification is a scoring system to assess the severity of liver cirrhosis

Score	1	2	3
Bilirubin ( $\mu\text{mol/l}$ )	<34	34-50	>50
Albumin (g/l)	>35	28-35	<28
Prothrombin time, prolonged by (s)	<4	4-6	>6
Encephalopathy	none	mild	marked
Ascites	none	mild	marked

Summation of the scores allows the severity to be graded either A, B or C:

- < 7 = A
- 7-9 = B
- > 9 = C

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Next

A 34-year-old woman with a history of alcohol excess is admitted with abdominal swelling to the Acute Medical Unit. A diagnosis of ascites secondary to liver cirrhosis is made and paracentesis is performed. The serum creatinine on admission is 95  $\mu\text{mol/l}$ . Ten days after admission urine output decreases significantly and blood tests reveal:

Na <sup>+</sup>	129 mmol/l
K <sup>+</sup>	3.7 mmol/l
Urea	14.2 mmol/l
Creatinine	221 $\mu\text{mol/l}$

Albumin is given to correct suspected hypovolaemia. What is the most appropriate further management?

- ☐ A. Octreotide
- ☐ B. Propranolol
- ☐ C. Terlipressin
- ☐ D. Acetylcysteine
- ☐ E. Dopamine

This patient has developed hepatorenal syndrome

**Hepatorenal syndrome: management**

The management of hepatorenal syndrome (HRS) is notoriously difficult. The ideal treatment is liver transplantation but patients are often too unwell to have surgery and there is a shortage of donors

Hepatorenal syndrome has been categorized into two types:

Type 1 HRS	Type 2 HRS
<ul style="list-style-type: none"><li>• Rapidly progressive</li><li>• Doubling of serum creatinine to <math>&gt; 221 \mu\text{mol/L}</math> or a halving of the creatinine clearance to less than 20 ml/min over a period of less than 2 weeks</li><li>• Very poor prognosis</li></ul>	<ul style="list-style-type: none"><li>• Slowly progressive</li><li>• Prognosis poor, but patients may live for longer</li></ul>

**Management options**

- vasopressin analogues, for example terlipressin, have a growing evidence base supporting their use. They work by causing vasoconstriction of the splanchnic circulation
- volume expansion with 20% albumin
- transjugular intrahepatic portosystemic shunt

A 29-year-old Russian man who has recently arrived into the country presents with fever and feeling generally unwell. His temperature is 38.2°C and pulse 96/min. On examination a grey coating is seen surrounding the tonsils and there is extensive cervical lymphadenopathy. What is the most likely diagnosis?

<input type="radio"/>	A. Dengue fever
<input type="radio"/>	B. Typhoid
<input type="radio"/>	C. Paratyphoid
<input type="radio"/>	D. Actinomycosis
<input type="radio"/>	E. Diphtheria

[Next question](#)

## Diphtheria

Diphtheria is caused by the Gram positive bacterium *Corynebacterium diphtheriae*

Diphtheria toxin commonly causes a 'diphtheric membrane' on tonsils caused by necrotic mucosal cells. Systemic distribution may produce necrosis of myocardial, neural and renal tissue

Possible presentations

- recent visitors to Eastern Europe/Russia/Asia
- bulky cervical lymphadenopathy
- neuritis e.g. cranial nerves
- heart block



A 29-year-old female is noted to have an elevated bilirubin during a viral illness. Gilbert's syndrome is suspected. Which one of the following tests may confirm the diagnosis?

<input type="radio"/>	A. Bromsulphthalein excretion test
<input type="radio"/>	B. Ammonium chloride acidification test
<input type="radio"/>	C. Urine analysis
<input type="radio"/>	D. Nicotinic acid test
<input type="radio"/>	E. Faecal fat excretion

[Next question](#)

### Gilbert's syndrome

Gilbert's syndrome is an autosomal recessive\* condition of defective bilirubin conjugation due to a deficiency of UDP glucuronyl transferase. The prevalence is approximately 1-2% in the general population

#### Features

- unconjugated hyperbilinaemia (i.e. not in urine)
- jaundice may only be seen during an intercurrent illness

#### Investigation and management

- investigation: rise in bilirubin following prolonged fasting or IV nicotinic acid
- no treatment required

\*the exact mode of inheritance is still a matter of debate

What percentage of patients with Peutz-Jeghers syndrome will have died from a related cancer by the age of 60 years?

<input type="radio"/>	A. 2-3%
<input type="radio"/>	B. 50%
<input type="radio"/>	C. 5-7%
<input type="radio"/>	D. >95%
<input type="radio"/>	E. 10-20%

[Next question](#)

### Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

#### Genetics

- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

#### Features

- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

#### Management

- conservative unless complications develop

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Next

A 45-year-old man with a history of alcoholic liver disease presents with abdominal distension. Examination reveals tense ascites which is drained. What is the appropriate type of diuretic to help prevent reaccumulation of ascites?

<input type="radio"/>	A. Aldosterone antagonist
<input type="radio"/>	B. Loop diuretic
<input type="radio"/>	C. Thiazide diuretic
<input type="radio"/>	D. Osmotic diuretic
<input type="radio"/>	E. Carbonic anhydrase inhibitor

Next question

Aldosterone antagonists such as spironolactone are used in high doses to help prevent the formation of ascites in patients with chronic liver disease. A loop diuretic may need to be added in patients who don't respond

**Spironolactone**

Spironolactone is an aldosterone antagonist which acts act in the distal convoluted tubule

**Indications**

- ascites: patients with cirrhosis develop a secondary hyperaldosteronism. Relatively large doses such as 100 or 200mg are often used
- heart failure (see RALES study below)
- nephrotic syndrome
- Conn's syndrome

**Adverse effects**

- hyperkalaemia
- gynaecomastia

**RALES**

- NYHA III + IV, patients already taking ACE inhibitor
- low dose spironolactone reduces all cause mortality

Which one of the following patients is most likely to require screening for hepatocellular carcinoma?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. A 45-year-old man with liver cirrhosis secondary to hepatitis C                                    |
| <input type="radio"/> | B. A 33-year-old man with HIV. He is taking antiretroviral therapy                                    |
| <input type="radio"/> | C. A 22-year-old man with alpha-1 antitrypsin deficiency. He has no evidence of current liver disease |
| <input type="radio"/> | D. A 52-year-old woman with alcohol-related liver cirrhosis who is still drinking                     |
| <input type="radio"/> | E. A 75-year-old man who drinks 100 units / week. He has no current signs of liver disease            |

Next question

Patients with liver cirrhosis secondary to hepatitis C have a 3-5% annual incidence of hepatocellular carcinoma.

### Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the third most common cause of cancer worldwide. Chronic hepatitis B is the most common cause of HCC worldwide with chronic hepatitis C being the most common cause in Europe.

The main risk factor for developing HCC is liver cirrhosis, for example secondary\* to hepatitis B & C, alcohol, haemochromatosis and primary biliary cirrhosis. Other risk factors include:

- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda
- male sex
- diabetes mellitus, metabolic syndrome

### Features

- tends to present late
- features of liver cirrhosis or failure may be seen: jaundice, ascites, RUQ pain, hepatomegaly, pruritus, splenomegaly
- possible presentation is decompensation in a patient with chronic liver disease

Screening with ultrasound (+/- alpha-fetoprotein) should be considered for high risk groups such as:

- patients liver cirrhosis secondary to hepatitis B & C or haemochromatosis
- men with liver cirrhosis secondary to alcohol

## Management options

- early disease: surgical resection
- liver transplantation
- radiofrequency ablation
- transarterial chemoembolisation
- sorafenib: a multikinase inhibitor

\*Wilson's disease is an exception

**Question 92 of 151**

Next

A 25-year-old intravenous drug user with chronic hepatitis C becomes pregnant. Approximately what is the chance of the virus being transmitted to her child?

<input type="radio"/>	A. <10%
<input type="radio"/>	B. 10-20%
<input type="radio"/>	C. 20-30%
<input type="radio"/>	D. 30-40%
<input type="radio"/>	E. 40-50%

Next question

**Hepatitis C**

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

**Transmission**

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

**Features**

- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

**Complications**

- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

**Management of chronic infection**

- currently a combination of pegylated interferon-alpha and ribavirin are used

- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains
- the aim of treatment is sustained virological response (SVR), defined as undetectable

serum HCV RNA six months after the end of therapy

#### Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

A 22-year-old man is investigated for weight loss and diarrhoea. A rectal biopsy is taken and reported as follows:

Deep inflammatory infiltrate from the mucosa to the lamina propria  
Numerous granulomata noted

What is the most likely diagnosis?

<input type="radio"/>	A. Crohn's disease
<input type="radio"/>	B. Rectal carcinoma-in-situ
<input type="radio"/>	C. Tuberculosis
<input type="radio"/>	D. Laxative abuse
<input type="radio"/>	E. Ulcerative colitis

Inflammation in ulcerative colitis is usually limited to the mucosa and submucosa.

### Crohn's disease: investigation

Crohn's disease is a form of inflammatory bowel disease. It commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus

#### Bloods

- C-reactive protein correlates well with disease activity

#### Endoscopy

- colonoscopy is the investigation of choice
- features suggest of Crohn's include deep ulcers, skip lesions

#### Histology

- inflammation in all layers from mucosa to serosa
- goblet cells
- granulomas

#### Small bowel enema

- high sensitivity and specificity for examination of the terminal ileum
- strictures: 'Kantor's string sign'
- proximal bowel dilation
- 'rose thorn' ulcers
- fistulae



A 59-year-old woman is admitted to the Emergency Department with a productive cough and pyrexia. She is usually fit and well but is undergoing investigation for dysphagia. This has been present for the past 3 months and affects both food and drink. A chest x-ray shows an air-fluid level behind a normal-sized heart. What is the most likely diagnosis?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Massive pericardial effusion |
| <input type="radio"/> | B. Tuberculosis                 |
| <input type="radio"/> | C. Achalasia                    |
| <input type="radio"/> | D. Pharyngeal pouch             |
| <input type="radio"/> | E. Hiatus hernia                |

A retrocardiac air-fluid level is sometimes seen in patients with achalasia

### Achalasia

Failure of oesophageal peristalsis and of relaxation of lower oesophageal sphincter (LOS) due to degenerative loss of ganglia from Auerbach's plexus i.e. LOS contracted, oesophagus above dilated. Achalasia typically presents in middle-age and is equally common in men and women.

#### Clinical features

- dysphagia of BOTH liquids and solids
- typically variation in severity of symptoms
- heartburn
- regurgitation of food - may lead to cough, aspiration pneumonia etc
- malignant change in small number of patients

#### Investigations

- manometry: excessive LOS tone which doesn't relax on swallowing - considered most important diagnostic test
- barium swallow shows grossly expanded oesophagus, fluid level
- CXR: wide mediastinum, fluid level

#### Treatment

- intra-sphincteric injection of botulinum toxin
- Heller cardiomyotomy
- balloon dilation
- drug therapy has a role but is limited by side-effects

A 31-year-old woman is reviewed in clinic. She has been referred by her GP with an 8 month history of abdominal discomfort associated with bloating. Which one of the following tests is it least useful to perform before making a positive diagnosis of irritable bowel syndrome?

<input type="radio"/>	A. Erythrocyte sedimentation rate
<input type="radio"/>	B. Thyroid function tests
<input type="radio"/>	C. Full blood count
<input type="radio"/>	D. C-reactive protein
<input type="radio"/>	E. Tissue transglutaminase antibodies

[Next question](#)

NICE recommends that thyroid function tests are not necessary prior to making a positive diagnosis of IBS. Erythrocyte sedimentation rate and C-reactive protein may help exclude inflammatory bowel disease.

### Irritable bowel syndrome: diagnosis

NICE published clinical guidelines on the diagnosis and management of irritable bowel syndrome (IBS) in 2008

The diagnosis of IBS should be considered if the patient has had the following for at least 6 months:

- abdominal pain, and/or
- bloating, and/or
- change in bowel habit

A positive diagnosis of IBS should be made if the patient has abdominal pain relieved by defecation or associated with altered bowel frequency stool form, in addition to 2 of the following 4 symptoms:

- altered stool passage (straining, urgency, incomplete evacuation)
- abdominal bloating (more common in women than men), distension, tension or hardness
- symptoms made worse by eating
- passage of mucus

Features such as lethargy, nausea, backache and bladder symptoms may also support the diagnosis

Red flag features should be enquired about:

- rectal bleeding
- unexplained/unintentional weight loss
- family history of bowel or ovarian cancer
- onset after 60 years of age

Suggested primary care investigations are:

- full blood count
- ESR/CRP
- coeliac disease screen (tissue transglutaminase antibodies)

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Next

A 43-year-old man is reviewed in the gastroenterology clinic. He has had troublesome dyspepsia for the past six months which has not settled with proton pump inhibitor therapy. During the review of systems he also reports passing 6-7 watery stools per day. An OGD 3 weeks ago showed gastric erosions and ulcers. Which one of the following investigations is most likely to be diagnostic?

<input type="radio"/>	A. Serum amylase
<input type="radio"/>	B. Urea breath test for <i>Helicobacter pylori</i>
<input type="radio"/>	C. Fasting gastrin
<input type="radio"/>	D. <sup>14</sup> C-xylose breath test
<input type="radio"/>	E. CT abdomen

Next question

CT abdomen has a sensitivity of only 50% for primary tumours in Zollinger-Ellison syndrome (ZES). Normal levels of fasting gastrin in untreated ZES are extremely rare

**Zollinger-Ellison syndrome**

Zollinger-Ellison syndrome is condition characterised by excessive levels of gastrin, usually from a gastrin secreting tumour usually of the duodenum or pancreas. Around 30% occur as part of MEN type I syndrome

**Features**

- multiple gastroduodenal ulcers
- diarrhoea
- malabsorption

**Diagnosis**

- fasting gastrin levels: the single best screen test
- secretin stimulation test

You are asked to review a 24-year-old man who has been admitted with an exacerbation of Crohn's disease. Despite prednisolone and mesalazine therapy for the past 3 weeks he is still passing 6-7 watery stools per day. He has lost a considerable amount of weight during this period. On examination he is afebrile, haemodynamically stable and his abdomen is soft and non-tender. What is the most appropriate next step?

<input type="radio"/>	A. Metronidazole
<input type="radio"/>	B. Infliximab
<input type="radio"/>	C. Methotrexate
<input type="radio"/>	D. Azathioprine
<input type="radio"/>	E. Surgery

### Crohn's disease: management

Crohn's disease is a form of inflammatory bowel disease. It commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus

#### General points

- patients should be strongly advised to stop smoking
- some studies suggest an increased risk of relapse secondary to NSAIDs and the combined oral contraceptive pill but the evidence is patchy

#### Active disease

- mesalazine: whilst evidence base is limited widely used in active disease
- steroids (oral, topical or intravenous)
- azathioprine is used as a second-line treatment in active disease
- methotrexate is used in patients intolerant of azathioprine or refractory disease. Usually given intramuscularly
- infliximab is useful in refractory disease and fistulating Crohn's. Patients typically continue on azathioprine or methotrexate

#### Perianal disease

- metronidazole is first-line

#### Enteral feeding with an elemental diet

- may be used in addition to or instead of other measures to induce remission

#### Surgery

- around 80% of patients with Crohn's disease will eventually have surgery

**Question 98 of 151**

Next

A 59-year-old female with a history of hypothyroidism presents with fatigue. Blood tests reveal the following:

Hb	9.4 g/dl
MCV	121 fl
Plt	$156 \times 10^9/l$
WBC	$4.3 \times 10^9/l$

What is the most appropriate investigation to perform next?

- ☐ A. Antral biopsy
- ☐ B. Bone marrow biopsy
- ☐ C. Lactate dehydrogenase
- ☐ D. Intrinsic factor antibodies
- ☐ E. Barium enema

Next question

Macrocytic anaemia in a patient with a history of hypothyroidism points towards a diagnosis of pernicious anaemia

**Pernicious anaemia: investigation**

## Investigation

- anti gastric parietal cell antibodies in 90% (but low specificity)
- anti intrinsic factor antibodies in 50% (specific for pernicious anaemia)
- macrocytic anaemia
- low WCC and platelets
- LDH may be raised due to ineffective erythropoiesis
- also low serum B12, hypersegmented polymorphs on film, megaloblasts in marrow
- Schilling test

## Schilling test

- radiolabelled B12 given on two occasions
- first on its own
- second with oral IF
- urine B12 levels measured

Which one of the following is least associated with hepatosplenomegaly?

<input type="radio"/>	A. Glandular fever
<input type="radio"/>	B. Chronic myeloid leukaemia
<input type="radio"/>	C. Alcoholic liver disease
<input type="radio"/>	D. Amyloidosis
<input type="radio"/>	E. Infective endocarditis

Next question

Infective endocarditis normally causes an isolated splenomegaly. Theoretically severe infective endocarditis may cause right heart failure and hence hepatomegaly but this would be unusual

### Hepatosplenomegaly

Causes of hepatosplenomegaly

- chronic liver disease\* with portal hypertension
- infections: glandular fever, malaria, hepatitis
- lymphoproliferative disorders
- myeloproliferative disorders e.g. CML
- amyloidosis

\*the latter stages of cirrhosis are associated with a small liver

Which one of the following is least associated with the development of colorectal cancer in patients with ulcerative colitis?

<input type="radio"/>	A. Unremitting disease
<input type="radio"/>	B. Disease duration > 10 years
<input type="radio"/>	C. Onset before 15 years old
<input type="radio"/>	D. Poor compliance to treatment
<input type="radio"/>	E. Disease confined to the rectum

[Next question](#)

### Ulcerative colitis: colorectal cancer

#### Overview

- risk of colorectal cancer is 10-20 times that of general population
- the increased risk is mainly related to chronic inflammation
- worse prognosis than patients without ulcerative colitis (partly due to delayed diagnosis)
- lesions may be multifocal

#### Factors increasing risk of cancer

- disease duration > 10 years
- patients with pancolitis
- onset before 15 years old
- unremitting disease
- poor compliance to treatment



A 44-year-old obese female is noted to have gallstones during an abdominal ultrasound, which was requested due to repeated urinary tract infections. Apart from the repeated UTIs she is otherwise well. What is the most appropriate management of the gallstones?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Ursodeoxycholic acid                                    |
| <input type="radio"/> | B. Extracorporeal Short Wave Lithotripsy                   |
| <input type="radio"/> | C. List for laparoscopic cholecystectomy when 50 years old |
| <input type="radio"/> | D. Observation   |
| <input type="radio"/> | E. List now for laparoscopic cholecystectomy               |

[Next question](#)

## Gallstones

Asymptomatic gallstones are common and do not require treatment

Which of the following conditions is least associated with *Helicobacter pylori*?

<input type="radio"/>	A. Gastric carcinoma
<input type="radio"/>	B. B cell lymphoma of MALT tissue
<input type="radio"/>	C. Gastro-oesophageal reflux disease
<input type="radio"/>	D. Atrophic gastritis
<input type="radio"/>	E. Peptic ulcer disease

Next question

### ***Helicobacter pylori***

*Helicobacter pylori* is a Gram negative bacteria associated with a variety of gastrointestinal problems, principally peptic ulcer disease

#### Associations

- peptic ulcer disease (95% of duodenal ulcers, 75% of gastric ulcers)
- gastric cancer
- B cell lymphoma of MALT tissue (eradication of H pylori results causes regression in 80% of patients)
- atrophic gastritis

The role of H pylori in Gastro-oesophageal reflux disease (GORD) is unclear - there is currently no role in GORD for the eradication of H pylori

Management - eradication may be achieved with a 7 day course of

- a proton pump inhibitor + amoxicillin + clarithromycin, or
- a proton pump inhibitor + metronidazole + clarithromycin

A 54-year-old man who is known to have gastric cancer is reviewed in clinic. He asks you about a rash he has developed. Which of the following skin disorders is most associated with gastric cancer?

- ☐ A. Erythema gyratum repens
- ☐ B. Necrolytic migratory erythema
- ☐ C. Sweet's syndrome
- ☐ D. Acquired ichthyosis
- ☐ E. Acanthosis nigricans

### Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	Associated malignancies
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Ovarian and lung cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

Each one of the following is associated with pancreatic cancer, except:

<input type="radio"/>	A. Chronic pancreatitis
<input type="radio"/>	B. Smoking
<input type="radio"/>	C. Blood group O
<input type="radio"/>	D. Diabetes
<input type="radio"/>	E. BRCA2 gene

Next question

## Pancreatic cancer

### Features

- classically painless jaundice
- however, patients typically present in a non-specific way with anorexia, weight loss, epigastric pain

### Associations

- smoking
- diabetes
- chronic pancreatitis
- hereditary pancreatitis
- hereditary non-polyposis colorectal carcinoma
- multiple endocrine neoplasia
- Peutz-Jeghers syndrome
- BRCA2
- dysplastic naevus syndrome

### Management

- less than 20% are suitable for surgery at diagnosis
- radio and chemotherapy are ineffective

A 36-year-old man presents with dyspepsia. No alarm symptoms are present. This is his first episode and he has no significant medical history of note. A test-and-treat strategy is agreed upon. What is the most appropriate investigation to test for *Helicobacter pylori*?

<input type="radio"/>	A. Gastric biopsy
<input type="radio"/>	B. CLO test (rapid urease test)
<input type="radio"/>	C. Stool culture
<input type="radio"/>	D. Hydrogen breath test
<input type="radio"/>	E. <sup>13</sup> C-urea breath test

[Next question](#)

The urea breath test is highly sensitive, specific and non-invasive. There is no indication for an endoscopy. Stool antigen, rather than culture, is an alternative.

### ***Helicobacter pylori*: tests**

#### Urea breath test

- patients consume a drink containing carbon isotope 13 (<sup>13</sup>C) enriched urea
- urea is broken down by *H. pylori* urease
- after 30 mins patient exhale into a glass tube
- mass spectrometry analysis calculates the amount of <sup>13</sup>C CO<sub>2</sub>
- should not be performed within 4 weeks of treatment with an antibacterial or within 2 weeks of an antisecretory drug (e.g. a proton pump inhibitor)
- sensitivity 95-98%, specificity 97-98%

#### Rapid urease test (e.g. CLO test)

- biopsy sample is mixed with urea and pH indicator
- colour change if *H. pylori* urease activity
- sensitivity 90-95%, specificity 95-98%

#### Serum antibody

- remains positive after eradication
- sensitivity 85%, specificity 80%

#### Culture of gastric biopsy

- provide information on antibiotic sensitivity

- sensitivity 70%, specificity 100%

#### Gastric biopsy

- histological evaluation alone, no culture
- sensitivity 95-99%, specificity 95-99%

#### Stool antigen test

- sensitivity 90%, specificity 95%

A 39-year-old man with a history of alcohol excess presents to the Emergency Department with a 2 day history of severe epigastric pain. His amylase is found to be 1260. What is the best marker of severity?

<input type="radio"/>	A. CRP
<input type="radio"/>	B. Amylase (on admission)
<input type="radio"/>	C. Pain scores
<input type="radio"/>	D. Lipase (on admission)
<input type="radio"/>	E. Number of similar previous admissions

[Next question](#)

CRP is now a widely used marker of severity in acute pancreatitis. Other methods which have to correlate with prognosis include the Ranson criteria and APACHE II score (Acute Physiology And Chronic Health Evaluation)

### Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RPC
- **D**rugs (azathioprine, mesalazine\*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

\*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

A 18-year-old male is admitted following after deliberately ingesting 40 grams of paracetamol. Twenty-four hours after admission he is reassessed with a view to liver transplantation. Of the following, which one would most strongly indicate the need for a liver transplant?

<input type="radio"/>	A. CRP 306
<input type="radio"/>	B. Arterial pH 7.25
<input type="radio"/>	C. Creatinine 267 $\mu\text{mol/l}$
<input type="radio"/>	D. Grade IV encephalopathy
<input type="radio"/>	E. INR 5.7

[Next question](#)

The arterial pH is the single most important factor. The creatinine, encephalopathy grade and INR must all be grossly abnormal otherwise

### Paracetamol overdose: management

#### Management

The following is based on the current BNF guidance. The National Poisons Information Service/TOXBASE should always be consulted for situations outside of the normal parameters.

Activated charcoal should be given if:

- paracetamol dose is in excess of 150 mg/kg (75 mg/kg if high-risk, see below) or 12 g, whichever is the smaller, and;
- the paracetamol was ingested in the previous hour

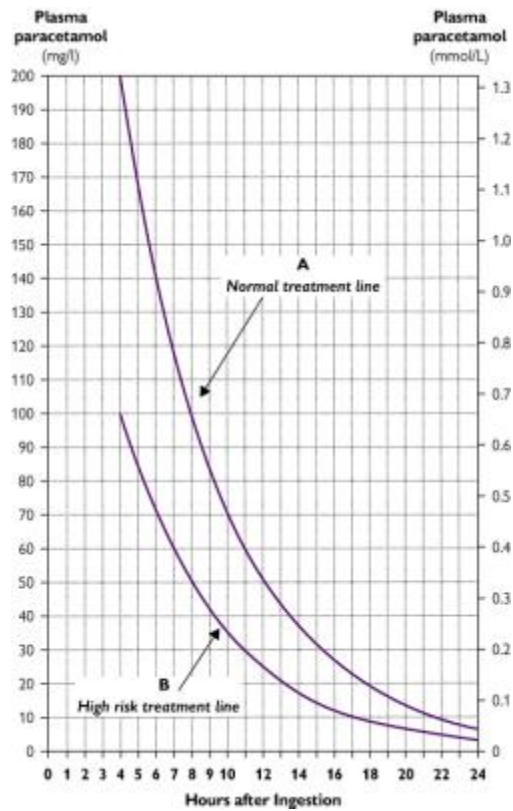
Patients presenting within 8 hours

- paracetamol levels (along with U&Es, LFTs and prothrombin time) should be checked 4 hours after ingestion (earlier samples may be misleading)
- the value should be plotted on a paracetamol treatment graph (see below)
- if the value is above the relevant treatment line intravenous acetylcysteine should be given

Patients presenting 8-24 hours after ingestion

- take an immediate blood sample for paracetamol levels, U&Es, LFTs and prothrombin time
- start acetylcysteine immediately if it is thought that more than 150 mg/kg body weight has been ingested. If the high risk (see below) consider treatment at a lower dose (75 mg/kg)
- otherwise wait for the paracetamol level, give intravenous acetylcysteine if the value is above the relevant treatment line





The following groups of patients are at an increased risk of developing hepatotoxicity following a paracetamol overdose and hence are considered 'high-risk':

- patients taking liver enzyme-inducing drugs (rifampicin, phenytoin, carbamazepine, chronic alcohol excess, St John's Wort)
- malnourished patients (e.g. anorexia or bulimia, cystic fibrosis, hepatitis C, alcoholism, HIV)
- patients who have not eaten for a few days

#### **King's College Hospital criteria for liver transplantation (paracetamol liver failure)**

Arterial pH < 7.3, 24 hours after ingestion

or all of the following:

- prothrombin time > 100 seconds
- creatinine > 300  $\mu\text{mol/l}$
- grade III or IV encephalopathy

A 44-year-old man is diagnosed with a right-sided colon cancer. He has a strong family history of colorectal and ovarian cancer. Genetic tests confirm a diagnosis of hereditary non-polyposis colorectal cancer (HNPCC) due to a defect in the MSH2 gene. What is the function of this gene?

- |                                  |                                     |
|----------------------------------|-------------------------------------|
| <input type="radio"/>            | A. Signal transduction              |
| <input type="radio"/>            | B. Apoptosis regulation             |
| <input type="radio"/>            | C. Epidermal growth factor receptor |
| <input checked="" type="radio"/> | D. DNA mismatch repair              |
| <input type="radio"/>            | E. Regulatory GTPase                |

[Next question](#)

### Colorectal cancer: genetics

It is currently thought there are three types of colon cancer:

- sporadic (95%)
- hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
- familial adenomatous polyposis (FAP, <1%)

Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene. It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC, an autosomal dominant condition, is the most common form of inherited colon cancer. Around 90% of patients develop cancers, often of the proximal colon, which are usually poorly differentiated and highly aggressive. Currently seven mutations have been identified, which affect genes involved in DNA mismatch repair leading to microsatellite instability. The most common genes involved are:

- MSH2 (60% of cases)
- MLH1 (30%)

The Amsterdam criteria are sometimes used to aid diagnosis:

- at least 3 family members with colon cancer
- the cases span at least two generations
- at least one case diagnosed before the age of 50 years

FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-40 years. Patients inevitably develop carcinoma. It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5. Genetic testing can be done by analysing DNA from a patient's white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.

Patients with FAP are also at risk from duodenal tumours. A variant of FAP called Gardner's syndrome can also feature osteomas of the skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on the skin

What percentage of patients with ulcerative colitis have primary sclerosing cholangitis?

- |                                  |         |
|----------------------------------|---------|
| <input type="radio"/>            | A. 0.5% |
| <input type="radio"/>            | B. 1%   |
| <input type="radio"/>            | C. 2%   |
| <input checked="" type="radio"/> | D. 4%   |
| <input type="radio"/>            | E. 10%  |

Next question

4% of patients with UC have PSC, 80% of patients with PSC have UC

### Primary sclerosing cholangitis

Primary sclerosing cholangitis is a biliary disease of unknown aetiology characterised by inflammation and fibrosis of intra and extra-hepatic bile ducts

#### Associations

- ulcerative colitis: 4% of patients with UC have PSC, 80% of patients with PSC have UC
- Crohn's (much less common association than UC)
- HIV

#### Features

- cholestasis: jaundice and pruritus
- right upper quadrant pain
- fatigue

#### Investigation

- ERCP is the standard diagnostic tool, showing multiple biliary strictures giving a 'beaded' appearance
- ANCA may be positive
- there is a limited role for liver biopsy, which may show fibrous, obliterative cholangitis often described as 'onion skin'

#### Complications

- cholangiocarcinoma (in 10%)
- increased risk of colorectal cancer

**Question 110 of 151**

Next

A 44-year-old man with alcoholic liver disease is admitted with pyrexia. He has been unwell for the past three days and has multiple previous admissions before with variceal bleeding. Examination shows multiple stigmata of chronic liver disease, ascites and jaundice. Paracentesis is performed with the following results:

Neutrophils	487 cells/ul
-------------	--------------

What is the most appropriate treatment?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Therapeutic abdominal washout          |
| <input type="radio"/> | B. Intravenous vancomycin + metronidazole |
| <input type="radio"/> | C. Intravenous cefotaxime                 |
| <input type="radio"/> | D. Insert an ascitic drain                |
| <input type="radio"/> | E. Intravenous ciprofloxacin              |

Next question

Spontaneous bacterial peritonitis - intravenous cefotaxime

Please see the British Society of Gastroenterology guidelines for more details.

**Spontaneous bacterial peritonitis**

Spontaneous bacterial peritonitis (SBP) is a form of peritonitis usually seen in patients with ascites secondary to liver cirrhosis.

**Diagnosis**

- paracentesis: neutrophil count > 250 cells/ul

**Management**

- intravenous cefotaxime is usually given
- patients who have had an episode of SBP should be on prophylactic antibiotics

Alcoholic liver disease is a marker of poor prognosis in SBP.

A 54-year-old female is admitted one week following a cholecystectomy with profuse diarrhoea. What is the most likely diagnosis?

<input type="radio"/>	A. <i>Campylobacter</i>
<input type="radio"/>	B. <i>E. coli</i>
<input type="radio"/>	C. <i>Clostridium difficile</i>
<input type="radio"/>	D. <i>Salmonella</i>
<input type="radio"/>	E. <i>Staphylococcus aureus</i>

[Next question](#)

*Clostridium difficile* is the most likely cause as the patient would have been given broad-spectrum antibiotics at the time of the operation

### ***Clostridium difficile***

*Clostridium difficile* is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading cause of *Clostridium difficile*.

#### Features

- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

#### Management

- first-line therapy is oral metronidazole for 10-14 days
- if severe or not responding to metronidazole then oral vancomycin may be used
- for life-threatening infections a combination of oral vancomycin and intravenous metronidazole should be used

A 29-year-old woman develops severe vomiting four hours after having lunch at a local restaurant. What is the most likely causative organism?

- ☐ A. *Escherichia coli*
- ☐ B. *Shigella*
- ☐ C. *Campylobacter*
- ☐ D. *Salmonella*
- ☐ E. *Staphylococcus aureus*

[Next question](#)

The short incubation period and severe vomiting point to a diagnosis of *Staphylococcus aureus* food poisoning.

### Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

### Stereotypical histories

<b><i>Escherichia coli</i></b>	Common amongst travellers Watery stools Abdominal cramps and nausea
<b>Giardiasis</b>	Prolonged, non-bloody diarrhoea
<b>Cholera</b>	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
<b><i>Shigella</i></b>	Bloody diarrhoea Vomiting and abdominal pain
<b><i>Staphylococcus aureus</i></b>	Severe vomiting Short incubation period
<b><i>Campylobacter</i></b>	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody

	Complications include Guillain-Barre syndrome
<b><i>Bacillus cereus</i></b>	Two types of illness are seen <ul style="list-style-type: none"> <li>• vomiting within 6 hours, stereotypically due to rice</li> <li>• diarrhoeal illness occurring after 6 hours</li> </ul>
<b>Amoebiasis</b>	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

#### Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus*\*
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

\*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours



A 39-year-old man with a history of liver cirrhosis secondary to alcohol excess is admitted with an upper gastrointestinal haemorrhage. He is treated with terlipressin and has an endoscopy with variceal band ligation 6 hours following admission. Which further intervention has been shown to reduce mortality during the acute admission?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. IV labetalol to induce hypotension for the first 3 days |
| <input type="radio"/> | B. Low-molecular weight heparin prophylaxis                |
| <input type="radio"/> | C. Nasogastric tube feeding for the first 3 days           |
| <input type="radio"/> | D. Antibiotic prophylaxis                                  |
| <input type="radio"/> | E. High-dose proton pump inhibitor therapy                 |

Next question

Antibiotic prophylaxis reduces mortality in cirrhotic patients with gastrointestinal bleeding

## Oesophageal varices

### Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent and is supported by NICE guidelines. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy. NICE recommend band ligation
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

### Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

A 26-year-old man with a history of speech and behavioural problems presents with lethargy. On examination he is noted to have jaundiced sclera. What is the most likely diagnosis?

<input type="radio"/>	A. Wiskott-Aldrich syndrome
<input type="radio"/>	B. Haemochromatosis
<input type="radio"/>	C. Friedreich's ataxia
<input type="radio"/>	D. Wilson's disease
<input type="radio"/>	E. Acute intermittent porphyria

### Wilson's disease

Wilson's disease is an autosomal recessive disorder characterised by excessive copper deposition in the tissues. Metabolic abnormalities include increased copper absorption from the small intestine and decreased hepatic copper excretion. Wilson's disease is caused by a defect in the ATP7B gene located on chromosome 13

The onset of symptoms is usually between 10 - 25 years. Children usually present with liver disease whereas the first sign of disease in young adults is often neurological disease

Features result from excessive copper deposition in the tissues, especially the brain, liver and cornea:

- liver: hepatitis, cirrhosis
- neurological: speech and behavioural problems are often the first manifestations. Also: excessive salivation, tremor, chorea
- Kayser-Fleischer rings
- renal tubular acidosis (esp. Fanconi syndrome)
- haemolysis
- blue nails

### Diagnosis

- reduced serum caeruloplasmin
- increased 24hr urinary copper excretion

### Management

- penicillamine (chelates copper) has been the traditional first-line treatment
- trientine hydrochloride is an alternative chelating agent which may become first-line treatment in the future
- tetrathiomolybdate is a newer agent that is currently under investigation

**Question 115 of 151**

Next

A 54-year-old man develops central abdominal pain a few hours after having an Endoscopic Retrograde Cholangiopancreatography (ERCP) performed. Investigations reveal the following:

Amylase	545 u/dl
---------	----------

Erect chest x-ray	Normal heart and lungs. No free air noted
-------------------	---

What is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Repeat ERCP + analgesia               |
| <input type="radio"/> | B. Reassure normal + analgesia           |
| <input type="radio"/> | C. Intravenous ciprofloxacin + analgesia |
| <input type="radio"/> | D. Surgical opinion + analgesia          |
| <input type="radio"/> | E. Intravenous fluids + analgesia        |

Next question

This patient has developed acute pancreatitis following ERCP and should be treated with intravenous fluids and analgesia.

Quinolones have not been shown to be beneficial in acute pancreatitis.

**Acute pancreatitis: causes**

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RPC
- **D**rugs (azathioprine, mesalazine\*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

\*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Which one of the following patients would it be most suitable to offer a screening test for coeliac disease to?

- ☐ A. A patient who is 'tired all the time'
- ☐ B. A patient with rheumatoid arthritis
- ☐ C. A patient who has a family history of inflammatory bowel disease
- ☐ D. A patient with type 2 diabetes mellitus
- ☐ E. A patient who develops erythema nodosum

[Next question](#)

### Coeliac disease

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis). It is strongly associated with HLA-DQ2 (95% of patients) and HLA-B8 (80%) as well as HLA-DR3 and HLA-DR7

In 2009 NICE issued guidelines on the investigation of coeliac disease. They suggest that the following patients should be screened for coeliac disease:

Signs and symptoms	Conditions
<ul style="list-style-type: none"> <li>Chronic or intermittent diarrhoea</li> <li>Failure to thrive or faltering growth (in children)</li> <li>Persistent or unexplained gastrointestinal symptoms including nausea and vomiting</li> <li>Prolonged fatigue ('tired all the time')</li> <li>Recurrent abdominal pain, cramping or distension</li> <li>Sudden or unexpected weight loss</li> <li>Unexplained iron-deficiency anaemia, or other unspecified anaemia</li> </ul>	<ul style="list-style-type: none"> <li>Autoimmune thyroid disease</li> <li>Dermatitis herpetiformis</li> <li>Irritable bowel syndrome</li> <li>Type 1 diabetes</li> <li>First-degree relatives (parents, siblings or children) with coeliac disease</li> </ul>

### Complications

- anaemia: iron, folate and vitamin B12 deficiency (folate deficiency is more common than vitamin B12 deficiency in coeliac disease)
- hyposplenism
- osteoporosis
- lactose intolerance
- enteropathy-associated T-cell lymphoma of small intestine
- subfertility, unfavourable pregnancy outcomes
- rare: oesophageal cancer, other malignancies

A 31-year-old man returns for review. He was diagnosed with an anal fissure around 7 weeks ago and has tried dietary modification, laxatives and topical anaesthetic with little benefit. What is the most appropriate next step?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Oral bisacodyl                                 |
| <input type="radio"/> | B. Oral calcium channel blocker                   |
| <input type="radio"/> | C. Topical steroid                                |
| <input type="radio"/> | D. Buccal glyceryl trinitrate prior to defecation |
| <input type="radio"/> | E. Topical glyceryl trinitrate                    |

[Next question](#)

Anal fissure - topical glyceryl trinitrate

### Anal fissure

Anal fissures are longitudinal or elliptical tears of the squamous lining of the distal anal canal. If present for less than 6 weeks they are defined as acute, and chronic if present for more than 6 weeks. Around 90% of anal fissures occur on the posterior midline

Management of an acute anal fissure (< 6 weeks)

- dietary advice: high-fibre diet with high fluid intake
- bulk-forming laxatives are first line - if not tolerated then lactulose should be tried
- lubricants such as petroleum jelly may be tried before defecation
- topical anaesthetics

-analgesia

- topical steroids do not provide significant relief

Management of a chronic anal fissure (> 6 weeks)

- the above techniques should be continued
- topical glyceryl trinitrate (GTN) is first line treatment for a chronic anal fissure
- if topical GTN is not effective after 8 weeks then secondary referral should be considered for surgery or botulinum toxin

Which one of the following features is least associated with ulcerative colitis?

<input type="radio"/>	A. Inflammatory cell infiltrate in the lamina propria
<input type="radio"/>	B. Pseudopolyps
<input type="radio"/>	C. Non-caseating granulomas
<input type="radio"/>	D. Depletion of goblet cells
<input type="radio"/>	E. Inflammation confined to the mucosa and submucosa

Next question

### IBD: histology

This histological differences between ulcerative colitis and Crohn's are summarised below:

#### Ulcerative colitis

- inflammation in mucosa and submucosa only (unless fulminant disease)
- widespread ulceration with preservation of adjacent mucosa which has the appearance of polyps ('pseudopolyps')
- inflammatory cell infiltrate in lamina propria
- crypt abscesses
- depletion of goblet cells and mucin from gland epithelium
- granulomas are infrequent

#### Crohn's

- inflammation occurs in all layers, down to the serosa. This predisposes to strictures, fistulas and adhesions
- oedema of mucosa and submucosa, combined with deep fissured ulcers ('rose-thorn') leads to a 'cobblestone' pattern
- lymphoid aggregates
- non-caseating granulomas

A 64-year-old woman complains of having 'excessive wind'. She is normally fit and well but for the past three months she has felt bloated and has been passing wind frequently. She also complains of vague upper abdominal pain and chronic diarrhoea. A hydrogen breath test confirms a diagnosis of small bowel bacterial overgrowth syndrome. What is the treatment of choice?

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. Tetracycline   |
| <input type="radio"/> | B. Rifaximin      |
| <input type="radio"/> | C. Cefaclor       |
| <input type="radio"/> | D. Nitrofurantoin |
| <input type="radio"/> | E. Ciprofloxacin  |

[Next question](#)

Tetracyclines are no longer commonly used due to widespread bacterial resistance.

### Small bowel bacterial overgrowth syndrome

Small bowel bacterial overgrowth syndrome (SBBOS) is a disorder characterised by excessive amounts of bacteria in the small bowel resulting in gastrointestinal symptoms.

#### Risk factors for SBBOS

- neonates with congenital gastrointestinal abnormalities
- scleroderma
- diabetes mellitus

It should be noted that many of the features overlap with irritable bowel syndrome:

- chronic diarrhoea
- bloating, flatulence
- abdominal pain

#### Diagnosis

- hydrogen breath test

#### Management

- correction of underlying disorder
- antibiotic therapy: rifaximin is now the treatment of choice due to relatively low resistance. Co-amoxiclav or metronidazole are also effective in the majority of patients.

A 25-year-old man presents with bloating and alteration in his bowel habit. He has been keeping a food diary and feels his symptoms may be secondary to a food allergy. Blood tests show a normal full blood count, ESR and thyroid function tests. Anti-endomysial antibodies are negative. What is the most suitable test to investigate possible food allergy?

- ☐ A. Total IgE levels
- ☐ B. Hair analysis
- ☐ C. Skin patch testing
- ☐ D. Skin prick test
- ☐ E. Jejunal biopsy

Next question

Skin prick testing would be first-line here as it is inexpensive and a large number of allergens can be investigated. Whilst there is a role for IgE testing in food allergy it is in the form of specific IgE antibodies rather than total IgE levels.

### Allergy tests

<b>Skin prick test</b>	<p>Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes</p> <p>Useful for food allergies and also pollen</p>
<b>Radioallergosorbent test (RAST)</b>	<p>Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive)</p> <p>Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom</p> <p>Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines</p>
<b>Skin patch testing</b>	<p>Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The patches are removed 48 hours later with the results being read by a dermatologist after a further 48 hours</p>



Autoimmune hepatitis is most characteristically associated with elevated levels of which one of the following immunoglobulins?

<input type="radio"/>	A. IgE
<input type="radio"/>	B. IgA
<input type="radio"/>	C. IgD
<input type="radio"/>	D. IgM
<input type="radio"/>	E. IgG

[Next question](#)

### Autoimmune hepatitis

Autoimmune hepatitis is condition of unknown aetiology which is most commonly seen in young females. Recognised associations include other autoimmune disorders, hypergammaglobulinaemia and HLA B8, DR3. Three types of autoimmune hepatitis have been characterised according to the types of circulating antibodies present

Type I	Type II	Type III
Anti-nuclear antibodies (ANA) and/or anti-smooth muscle antibodies (SMA)	Anti-liver/kidney microsomal type 1 antibodies (LKM1)	Soluble liver-kidney antigen
Affects both adults and children	Affects children only	Affects adults in middle-age

### Features

- may present with signs of chronic liver disease
- acute hepatitis: fever, jaundice etc (only 25% present in this way)
- amenorrhoea (common)
- ANA/SMA/LKM1 antibodies, raised IgG levels
- liver biopsy: inflammation extending beyond limiting plate 'piecemeal necrosis', bridging necrosis

### Management

- steroids, other immunosuppressants e.g. azathioprine
- liver transplantation

The action of which one of the following brush border enzymes results in the formation of glucose and galactose?

<input type="radio"/>	A. Dipeptidase
<input type="radio"/>	B. A-dextrinase
<input type="radio"/>	C. Maltase
<input checked="" type="radio"/>	D. Lactase
<input type="radio"/>	E. Sucrase

[Next question](#)

Brush border enzymes:

- maltase: glucose + glucose
- sucrase: glucose + fructose
- lactase: glucose + galactose

### Gastrointestinal physiology: enzymes

Amylase is present in saliva and pancreatic secretions. It breaks starch down into sugar

The following brush border enzymes are involved in the breakdown of carbohydrates:

- maltase: cleaves disaccharide maltose to glucose + glucose
- sucrase: cleaves sucrose to fructose and glucose
- lactase: cleaves disaccharide lactose to glucose + galactose

A 31-year-old woman who initially presented with abdominal pain and constipation is diagnosed with irritable bowel syndrome. Which one of the following bits of dietary advice is it least suitable to give?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Avoid missing meals   |
| <input type="radio"/> | B. Restrict tea and coffee to 3 cups per day                     |
| <input type="radio"/> | C. Increase the intake of fibre such as bran and wholemeal bread |
| <input type="radio"/> | D. Reduce intake of alcohol                                      |
| <input type="radio"/> | E. Drink at least 8 cups of fluid per day                        |

[Next question](#)

Insoluble sources of fibre such as bran and wholemeal should be avoided in IBS

### Irritable bowel syndrome: management

The management of irritable bowel syndrome (IBS) is often difficult and varies considerably between patients. NICE issued guidelines in 2008

First-line pharmacological treatment - according to predominant symptom

- pain: antispasmodic agents
- constipation: laxatives but avoid lactulose
- diarrhoea: loperamide is first-line

Second-line pharmacological treatment

- low-dose tricyclic antidepressants (e.g. amitriptyline 5-10 mg) are used in preference to selective serotonin reuptake inhibitors

Other management options

- psychological interventions - if symptoms do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile (refractory IBS), consider referring for cognitive behavioural therapy, hypnotherapy or psychological therapy
- complementary and alternative medicines: 'do not encourage use of acupuncture or reflexology for the treatment of IBS'

## General dietary advice

- have regular meals and take time to eat
- avoid missing meals or leaving long gaps between eating
- drink at least 8 cups of fluid per day, especially water or other non-caffeinated drinks such as herbal teas
- restrict tea and coffee to 3 cups per day
- reduce intake of alcohol and fizzy drinks
- consider limiting intake of high-fibre food (for example, wholemeal or high-fibre flour and breads, cereals high in bran, and whole grains such as brown rice)
- reduce intake of 'resistant starch' often found in processed foods
- limit fresh fruit to 3 portions per day
- for diarrhoea, avoid sorbitol
- for wind and bloating consider increasing intake of oats (for example, oat-based

breakfast cereal or porridge) and linseeds (up to one tablespoon per day).

What percentage of patients who contract the hepatitis C virus will become chronically infected?

- |                                  |           |
|----------------------------------|-----------|
| <input type="radio"/>            | A. 30-35% |
| <input checked="" type="radio"/> | B. 80-85% |
| <input type="radio"/>            | C. 65-70% |
| <input type="radio"/>            | D. 5-10%  |
| <input type="radio"/>            | E. 15-20% |

Next question

Hepatitis C - 80-85% become chronically infected

## Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

### Transmission

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

### Features

- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

### Complications

- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

## Management of chronic infection

- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains
- the aim of treatment is sustained virological response (SVR), defined as undetectable

serum HCV RNA six months after the end of therapy

## Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

Which one of the following is not associated with non-alcoholic steatohepatitis?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Hyperlipidaemia                  |
| <input type="radio"/> | B. Obesity                          |
| <input type="radio"/> | C. Sudden weight loss or starvation |
| <input type="radio"/> | D. Jejunioileal bypass              |
| <input type="radio"/> | E. Type 1 diabetes mellitus         |

Next question

Obese T2DM with abnormal LFTs - ? non-alcoholic fatty liver disease

### Non-alcoholic fatty liver disease

Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in the developed world. It is largely caused by obesity and describes a spectrum of disease ranging from:

- steatosis - fat in the liver
- steatohepatitis - fat with inflammation, non-alcoholic steatohepatitis (NASH), see below
- progressive disease may cause fibrosis and liver cirrhosis

NAFLD is thought to represent the hepatic manifestation of the metabolic syndrome and hence insulin resistance is thought to be the key mechanism leading to steatosis

Non-alcoholic steatohepatitis (NASH) is a term used to describe liver changes similar to those seen in alcoholic hepatitis in the absence of a history of alcohol abuse. It is relatively common and thought to affect around 3-4% of the general population. The progression of disease in patients with NASH may be responsible for a proportion of patients previously labelled as cryptogenic cirrhosis

Associated factors

- obesity
- hyperlipidaemia
- type 2 diabetes mellitus
- jejunioileal bypass
- sudden weight loss/starvation

## Features

- usually asymptomatic
- hepatomegaly
- ALT is typically greater than AST
- increased echogenicity on ultrasound

## Management

- the mainstay of treatment is lifestyle changes (particularly weight loss) and monitoring
- there is ongoing research into the role of gastric banding and insulin-sensitising drugs (e.g. Metformin)



A 30-year-old woman presents with abdominal pain that is associated with alternating diarrhoea and constipation. Which one of the following symptoms is least consistent with a diagnosis of irritable bowel syndrome?

<input type="radio"/>	A. Feeling of incomplete stool evacuation
<input type="radio"/>	B. Waking at night due to the pain
<input type="radio"/>	C. Abdominal bloating
<input type="radio"/>	D. Faecal urgency
<input type="radio"/>	E. Passage of mucous with stool

[Next question](#)

Pain which wakes a patient at night is not a feature that would be expected in irritable bowel syndrome.

### Irritable bowel syndrome: diagnosis

NICE published clinical guidelines on the diagnosis and management of irritable bowel syndrome (IBS) in 2008

The diagnosis of IBS should be considered if the patient has had the following for at least 6 months:

- abdominal pain, and/or
- bloating, and/or
- change in bowel habit

A positive diagnosis of IBS should be made if the patient has abdominal pain relieved by defecation or associated with altered bowel frequency stool form, in addition to 2 of the following 4 symptoms:

- altered stool passage (straining, urgency, incomplete evacuation)
- abdominal bloating (more common in women than men), distension, tension or hardness
- symptoms made worse by eating
- passage of mucus

Features such as lethargy, nausea, backache and bladder symptoms may also support the diagnosis

Red flag features should be enquired about:

- rectal bleeding
- unexplained/unintentional weight loss
- family history of bowel or ovarian cancer
- onset after 60 years of age

Suggested primary care investigations are:

- full blood count
- ESR/CRP
- coeliac disease screen (tissue transglutaminase antibodies)

A 30-year-old woman is investigated for chronic diarrhoea, bloating and tiredness. A diagnosis of coeliac disease is suspected. Which one of the following factors would increase the likelihood of a false negative serology test?

<input type="radio"/>	A. Hyposplenism
<input type="radio"/>	B. Being on a gluten free diet for one week prior to the test
<input type="radio"/>	C. A course of prednisolone one week prior to the test
<input type="radio"/>	D. The presence of dermatitis herpetiformis
<input type="radio"/>	E. Selective IgA deficiency

Selective IgA deficiency is more common in patients with coeliac disease. For this reason IgA levels should be checked when serological tests are ordered. If the patient has selective IgA deficiency tissue transglutaminase IgG can be measured.

Patients normally need to be following a gluten-free diet for at least 6 months before the serology becomes negatives.

### Coeliac disease: investigation

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis).

Diagnosis is made by a combination of immunology and jejunal biopsy. Villous atrophy and immunology normally reverses on a gluten-free diet.

NICE issued guidelines on the investigation of coeliac disease in 2009. If patients are already taking a gluten-free diet they should be asked, if possible, to reintroduce gluten for at least 6 weeks prior to testing.

#### Immunology

- tissue transglutaminase (TTG) antibodies (IgA) are first-choice according to NICE
- endomyseal antibody (IgA)
- anti-gliadin antibody (IgA or IgG) tests are not recommended by NICE
- anti-casein antibodies are also found in some patients

#### Jejunal biopsy

- villous atrophy
- crypt hyperplasia
- increase in intraepithelial lymphocytes
- lamina propria infiltration with lymphocytes

Rectal gluten challenge has been described but is not widely used

**Question 128 of 151**

Next

A 70-year-old man who is known to have atrial fibrillation presents with abdominal pain and rectal bleeding. A diagnosis of ischaemic colitis is suspected. Which part of the colon is most likely to be affected?

<input type="radio"/>	A. Hepatic flexure
<input type="radio"/>	B. Descending colon
<input type="radio"/>	C. Splenic flexure
<input type="radio"/>	D. Ascending colon
<input type="radio"/>	E. Rectum

Next question

**Mesenteric ischaemia**

Mesenteric ischaemia is primarily caused by arterial embolism resulting in infarction of the colon. It is more likely to occur in areas such as the splenic flexure that are located at the borders of the territory supplied by the superior and inferior mesenteric arteries.

**Predisposing factors**

- increasing age
- atrial fibrillation
- other causes of emboli: endocarditis
- cardiovascular disease risk factors: smoking, hypertension, diabetes

**Features**

- abdominal pain
- rectal bleeding
- diarrhoea
- fever
- bloods typically show an elevated WBC associated with acidosis

**Management**

- supportive care
- laparotomy and bowel resection

**Question 129 of 151**

Next

A 23-year-old female with a history of diarrhoea and weight loss has a colonoscopy to investigate her symptoms. A biopsy is taken and reported as follows:

Pigment laden macrophages

What is the most likely diagnosis?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Intestinal melanoma |
| <input type="radio"/> | B. Haemochromatosis    |
| <input type="radio"/> | C. Ulcerative colitis  |
| <input type="radio"/> | D. Laxative abuse      |
| <input type="radio"/> | E. Colorectal cancer   |

Next question

Diarrhoea - biopsy shows pigment laden macrophages = laxative abuse

**Melanosis coli**

Melanosis coli is a disorder of pigmentation of the bowel wall. Histology demonstrates pigment-laden macrophages

It is associated with laxative abuse, especially anthraquinone compounds such as senna

A patient who was an intravenous drug user in the 1990s asks for a hepatitis C test. What is the most appropriate action?

<input type="radio"/>	A. Refer him for pre-test counselling to discuss the pros and cons of testing
<input type="radio"/>	B. Advise him that no accurate test is currently available but that he should undertake normal precautions
<input type="radio"/>	C. Arrange an anti-HCV antibody test
<input type="radio"/>	D. Arrange a HCV RNA test
<input type="radio"/>	E. Refer him to gastroenterology for a liver biopsy

[Next question](#)

HCV RNA tests are normally only ordered following a positive antibody test.

## Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

### Transmission

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

### Features

- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

### Complications

- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
- cryoglobulinaemia

## Management of chronic infection

- currently a combination of pegylated interferon-alpha and ribavirin are used
- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains
- the aim of treatment is sustained virological response (SVR), defined as undetectable

serum HCV RNA six months after the end of therapy

## Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

What percentage of cases of chronic pancreatitis in the UK are due to alcohol excess?

<input type="radio"/>	A.	35%
<input type="radio"/>	B.	50%
<input type="radio"/>	C.	65%
<input checked="" type="radio"/>	D.	80%
<input type="radio"/>	E.	95%

Next question

### Chronic pancreatitis

Chronic pancreatitis is an inflammatory condition which can ultimately affect both the exocrine and endocrine functions of the pancreas. Around 80% of cases are due to alcohol excess with up to 20% of cases being unexplained

#### Features

- pain is typically worse 15 to 30 minutes following a meal
- steatorrhea: symptoms of pancreatic insufficiency usually develop between 5 and 25 years after the onset of pain
- diabetes mellitus develops in the majority of patients. It typically occurs more than 20 years after symptom begin

#### Investigation

- abdominal x-ray shows pancreatic calcification in 30% of cases
- CT is more sensitive at detecting pancreatic calcification. Sensitivity is 80%, specificity is 85%
- functional tests: faecal elastase may be used to assess exocrine function if imaging inconclusive

#### Management

- pancreatic enzyme supplements
- analgesia
- antioxidants: limited evidence base - one study suggests benefit in early disease



A 28-year-old woman is diagnosed with constipation predominant irritable bowel syndrome. She occasionally experiences spasms of pain in the left iliac fossa. Which one of the following is least likely to help her symptoms?

- |                       |                    |
|-----------------------|--------------------|
| <input type="radio"/> | A. Mebeverine      |
| <input type="radio"/> | B. Ispaghula       |
| <input type="radio"/> | C. Methylcellulose |
| <input type="radio"/> | D. Sterculia       |
| <input type="radio"/> | E. Lactulose       |

[Next question](#)

NICE recommend avoiding lactulose in the management of IBS

### Irritable bowel syndrome: management

The management of irritable bowel syndrome (IBS) is often difficult and varies considerably between patients. NICE issued guidelines in 2008

First-line pharmacological treatment - according to predominant symptom

- pain: antispasmodic agents
- constipation: laxatives but avoid lactulose
- diarrhoea: loperamide is first-line

Second-line pharmacological treatment

- low-dose tricyclic antidepressants (e.g. amitriptyline 5-10 mg) are used in preference to selective serotonin reuptake inhibitors

Other management options

- psychological interventions - if symptoms do not respond to pharmacological treatments after 12 months and who develop a continuing symptom profile (refractory IBS), consider referring for cognitive behavioural therapy, hypnotherapy or psychological therapy
- complementary and alternative medicines: 'do not encourage use of acupuncture or reflexology for the treatment of IBS'

## General dietary advice

- have regular meals and take time to eat
- avoid missing meals or leaving long gaps between eating
- drink at least 8 cups of fluid per day, especially water or other non-caffeinated drinks such as herbal teas
- restrict tea and coffee to 3 cups per day
- reduce intake of alcohol and fizzy drinks
- consider limiting intake of high-fibre food (for example, wholemeal or high-fibre flour and breads, cereals high in bran, and whole grains such as brown rice)
- reduce intake of 'resistant starch' often found in processed foods
- limit fresh fruit to 3 portions per day
- for diarrhoea, avoid sorbitol
- for wind and bloating consider increasing intake of oats (for example, oat-based

breakfast cereal or porridge) and linseeds (up to one tablespoon per day).

**Question 133 of 151**

Next

A 23-year-old who is 10 weeks pregnant is reviewed by the midwife at the booking visit. This is her first pregnancy and she is well apart from some sickness which is worse in the morning and a generalised pruritus. Bloods tests including the full blood count, hepatitis B, C and HIV serology are normal. A slight yellow tinge of her sclera is noticed and liver function tests are ordered:

Bilirubin	42 $\mu$ mol/L
ALP	160 U/L
ALT	25 U/L
Albumin	34 g/L

What is the most likely diagnosis?

- ☐ A. Gilbert's syndrome
- ☐ B. Gallstones
- ☐ C. Acute fatty liver
- ☐ D. Intrahepatic cholestasis of pregnancy
- ☐ E. Primary biliary cirrhosis

Next question

Morning sickness and pruritus are common in pregnant women. Intrahepatic cholestasis of pregnancy would not occur in the first trimester. An ALP of 160 U/l is normal in a pregnant woman leaving the only abnormal result being the raised bilirubin (which usually falls in pregnancy). The most likely diagnosis is therefore Gilbert's syndrome.

**Gilbert's syndrome**

Gilbert's syndrome is an autosomal recessive\* condition of defective bilirubin conjugation due to a deficiency of UDP glucuronyl transferase. The prevalence is approximately 1-2% in the general population

**Features**

- unconjugated hyperbilinaemia (i.e. not in urine)
- jaundice may only be seen during an intercurrent illness

**Investigation and management**

- investigation: rise in bilirubin following prolonged fasting or IV nicotinic acid
- no treatment required

\*the exact mode of inheritance is still a matter of debate

Which one of the following statements regarding hepatocellular carcinoma is correct?

<input type="radio"/>	A. Diabetes mellitus is a risk factor
<input type="radio"/>	B. Screening has not been shown to be effective
<input type="radio"/>	C. Bevacizumab may be used for advanced cases
<input type="radio"/>	D. The incidence is significantly higher in women
<input type="radio"/>	E. Alcohol excess is the most common underlying cause worldwide

Next question

### Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the third most common cause of cancer worldwide. Chronic hepatitis B is the most common cause of HCC worldwide with chronic hepatitis C being the most common cause in Europe.

The main risk factor for developing HCC is liver cirrhosis, for example secondary\* to hepatitis B & C, alcohol, haemochromatosis and primary biliary cirrhosis. Other risk factors include:

- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda
- male sex
- diabetes mellitus, metabolic syndrome

### Features

- tends to present late
- features of liver cirrhosis or failure may be seen: jaundice, ascites, RUQ pain, hepatomegaly, pruritus, splenomegaly
- possible presentation is decompensation in a patient with chronic liver disease

Screening with ultrasound (+/- alpha-fetoprotein) should be considered for high risk groups such as:

- patients liver cirrhosis secondary to hepatitis B & C or haemochromatosis
- men with liver cirrhosis secondary to alcohol

## Management options

- early disease: surgical resection
- liver transplantation
- radiofrequency ablation
- transarterial chemoembolisation
- sorafenib: a multikinase inhibitor

\*Wilson's disease is an exception

Which one of the following is least associated with primary biliary cirrhosis?

<input type="radio"/>	A. Ulcerative colitis
<input type="radio"/>	B. Systemic sclerosis
<input type="radio"/>	C. Thyroid disease
<input type="radio"/>	D. Sjogren's syndrome
<input type="radio"/>	E. Rheumatoid arthritis

Next question

Whilst ulcerative colitis is associated with primary biliary cirrhosis this is less common than the other four options

Primary sclerosing cholangitis is strongly associated with ulcerative colitis

### Primary biliary cirrhosis

Primary biliary cirrhosis is a chronic liver disorder typically seen in middle-aged females (female:male ratio of 9:1). The aetiology is not fully understood although it is thought to be an autoimmune condition. Interlobular bile ducts become damaged by a chronic inflammatory process causing progressive cholestasis which may eventually progress to cirrhosis. The classic presentation is itching in a middle-aged woman

#### Associations

- Sjogren's syndrome (seen in up to 80% of patients)
- rheumatoid arthritis
- systemic sclerosis
- thyroid disease

#### Diagnosis

- anti-mitochondrial antibodies (AMA) M2 subtype are present in 98% of patients and are highly specific
- smooth muscle antibodies in 30% of patients
- raised serum IgM

#### Management

- pruritus: cholestyramine
- fat-soluble vitamin supplementation
- ursodeoxycholic acid
- liver transplantation e.g. if bilirubin > 100 (PBC is a major indication) - recurrence in graft can occur but is not usually a problem

A 72-year-old female is admitted with diarrhoea to the acute medical unit. A sigmoidoscopy is performed which shows multiple white plaques adhered to the gastrointestinal mucosa. What is the most likely diagnosis?

<input type="radio"/>	A. Crohn's disease
<input type="radio"/>	B. Ulcerative colitis
<input type="radio"/>	C. Ischaemic colitis
<input type="radio"/>	D. Pseudomembranous colitis
<input type="radio"/>	E. Colorectal cancer

[Next question](#)

### ***Clostridium difficile***

*Clostridium difficile* is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading cause of *Clostridium difficile*.

#### Features

- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

#### Management

- first-line therapy is oral metronidazole for 10-14 days
- if severe or not responding to metronidazole then oral vancomycin may be used
- for life-threatening infections a combination of oral vancomycin and intravenous metronidazole should be used

You are reviewing a 31-year-old man in the liver clinic. He is currently on interferon-alpha treatment. What is the best way to assess his response to treatment?

<input type="radio"/>	A. Alanine transaminase level
<input type="radio"/>	B. Anti-HCV antibodies
<input type="radio"/>	C. Viral load
<input type="radio"/>	D. Prothrombin time
<input type="radio"/>	E. Hepatitis C genotype

[Next question](#)

## Hepatitis C

Hepatitis C is likely to become a significant public health problem in the UK in the next decade. It is thought around 200,000 people are chronically infected with the virus. At risk groups include intravenous drug users and patients who received a blood transfusion prior to 1991 (e.g. haemophiliacs).

### Transmission

- the risk of transmission during a needle stick injury is about 2%
- the vertical transmission rate from mother to child is about 6%
- breast feeding is not contraindicated in mothers with hepatitis C
- the risk of transmitting the virus during sexual intercourse is probably less than 5%

### Features

- after exposure to the hepatitis C virus less than 20% of patients develop an acute hepatitis

### Complications

- chronic infection (80-85%) - only 15-20% of patients will clear the virus after an acute infection and hence the majority will develop chronic hepatitis C
- cirrhosis (20-30% of those with chronic disease)
- hepatocellular cancer
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### Management of chronic infection

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- up to 55% of patients successfully clear the virus, with success rates of around 80% for some strains
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serum HCV RNA six months after the end of therapy

#### Complications of treatment

- ribavirin - side-effects: haemolytic anaemia, cough. Women should not become pregnant within 6 months of stopping ribavirin as it is teratogenic
- interferon alpha - side-effects: flu-like symptoms, depression, fatigue, leukopenia, thrombocytopenia

What percentage of patients with chronic hepatitis C will develop liver cirrhosis over a 20-30 year period?

<input type="radio"/>	A.	5-10%
<input type="radio"/>	B.	10-20%
<input type="radio"/>	C.	20-30%
<input type="radio"/>	D.	40-50%
<input type="radio"/>	E.	60-70%

Next question

Liver cirrhosis will develop in around 20-30% of patients over 20-30 years

## Hepatitis C

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Which one of the following is most strongly associated with coeliac disease?

- ☐ A. HLA A5
- ☐ B. HLA-DQ2
- ☐ C. HLA-DR2
- ☐ D. HLA-DR4
- ☐ E. HLA-B27

### Coeliac disease

Coeliac disease is caused by sensitivity to the protein gluten. Repeated exposure leads to villous atrophy which in turn causes malabsorption. Conditions associated with coeliac disease include dermatitis herpetiformis (a vesicular, pruritic skin eruption) and autoimmune disorders (type 1 diabetes mellitus and autoimmune hepatitis). It is strongly associated with HLA-DQ2 (95% of patients) and HLA-B8 (80%) as well as HLA-DR3 and HLA-DR7

In 2009 NICE issued guidelines on the investigation of coeliac disease. They suggest that the following patients should be screened for coeliac disease:

Signs and symptoms	Conditions
<ul style="list-style-type: none"> <li>Chronic or intermittent diarrhoea</li> <li>Failure to thrive or faltering growth (in children)</li> <li>Persistent or unexplained gastrointestinal symptoms including nausea and vomiting</li> <li>Prolonged fatigue ('tired all the time')</li> <li>Recurrent abdominal pain, cramping or distension</li> <li>Sudden or unexpected weight loss</li> <li>Unexplained iron-deficiency anaemia, or other unspecified anaemia</li> </ul>	<ul style="list-style-type: none"> <li>Autoimmune thyroid disease</li> <li>Dermatitis herpetiformis</li> <li>Irritable bowel syndrome</li> <li>Type 1 diabetes</li> <li>First-degree relatives (parents, siblings or children) with coeliac disease</li> </ul>

### Complications

- anaemia: iron, folate and vitamin B12 deficiency (folate deficiency is more common than vitamin B12 deficiency in coeliac disease)
- hyposplenism
- osteoporosis
- lactose intolerance
- enteropathy-associated T-cell lymphoma of small intestine
- subfertility, unfavourable pregnancy outcomes
- rare: oesophageal cancer, other malignancies

Which one of the following statements regarding hepatitis B and pregnancy is correct?

<input type="radio"/>	A. Without intervention the vertical transmission rate is around 3%
<input type="radio"/>	B. Only at risk groups should be screened for hepatitis B during pregnancy
<input type="radio"/>	C. Around 30% of mothers with hepatitis B develop pre-eclampsia
<input type="radio"/>	D. It is safe for a mother with hepatitis B to breastfeed her newborn
<input type="radio"/>	E. All pregnant women with hepatitis B should take oral ribavirin in the last trimester of pregnancy

Next question

Without intervention the vertical transmission rate is around 20%, which increases to 90% if the woman is positive for HBeAg.

### Hepatitis B and pregnancy

#### Basics

- all pregnant women are offered screening for hepatitis B
- babies born to mothers who are chronically infected with hepatitis B or to mothers who've had acute hepatitis B during pregnancy should receive a complete course of vaccination + hepatitis B immunoglobulin
- studies are currently evaluating the role of oral antiviral treatment (e.g. Lamivudine) in the latter part of pregnancy
- there is little evidence to suggest caesarean section reduces vertical transmission rates
- hepatitis B cannot be transmitted via breastfeeding (in contrast to HIV)

A 68-year-old woman comes back to rheumatology clinic for review. Two weeks ago she was referred with pain in her left knee and the clinical impression at the time was osteoarthritis. As her pain was not responding to paracetamol she was commenced on diclofenac 50mg tds and lansoprazole 30mg od. Shortly afterwards she developed some indigestion which seems to resolve if she skips the diclofenac dose. She is otherwise asymptomatic and got good pain relief from diclofenac. Clinical examination is normal. What is the most appropriate action?

<input type="radio"/>	A. <sup>13</sup> C-urea breath test
<input type="radio"/>	B. Stop diclofenac, continue lansoprazole + review in 1 week
<input type="radio"/>	C. Switch diclofenac to ibuprofen, continue lansoprazole
<input type="radio"/>	D. Urgent endoscopy
<input type="radio"/>	E. Admit

[Next question](#)

When NICE first published their dyspepsia guidelines there was a policy of referral for any older patients with new onset dyspepsia. This led to a deluge of referrals and amended guidelines were published in 2004. This modified approach seems to be supported by a large trial demonstrating a minimal effect on mortality of routine referral.

This question gives an example of a scenario where NICE would recommend not initially referring a patient when there is an obvious trigger (NSAID use).

## Dyspepsia

In 2004 NICE published guidelines for the management of dyspepsia in primary care. These take into account the age of the patient (whether younger or older than 55 years) and the presence or absence of 'alarm signs':

- chronic gastrointestinal bleeding
- progressive unintentional weight loss
- progressive difficulty swallowing
- persistent vomiting
- iron deficiency anaemia
- epigastric mass
- suspicious barium meal

### Deciding whether urgent referral for endoscopy is needed

Urgent referral (within 2 weeks) is indicated for patients with any alarm signs irrespective of age

Routine endoscopic investigation of patients of any age, presenting with dyspepsia and without alarm signs is not necessary, however

Patients aged 55 years and over should be referred urgently for endoscopy if dyspepsia symptoms are:

- recent in onset rather than recurrent and
- unexplained (e.g. New symptoms which cannot be explained by precipitants such as NSAIDs) and
- persistent: continuing beyond a period that would normally be associated with self-limiting problems (e.g. Up to four to six weeks, depending on the severity of signs and symptoms)

### **Managing patients who do not meet referral criteria ('undiagnosed dyspepsia')**

This can be summarised at a step-wise approach

- 1. Review medications for possible causes of dyspepsia
- 2. Lifestyle advice
- 3. Trial of full-dose PPI for one month\*
- 4. 'Test and treat' using carbon-13 urea breath test

\*it is unclear from studies whether a trial of a PPI or a 'test and treat' should be used first

Which one of the following is most associated with oesophageal cancer?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Coeliac disease    |
| <input type="radio"/> | B. Hypothyroidism     |
| <input type="radio"/> | C. Crohn's disease    |
| <input type="radio"/> | D. Addison's disease  |
| <input type="radio"/> | E. Ulcerative colitis |

Next question

### Oesophageal cancer

Until recent times oesophageal cancer was most commonly due to a squamous cell carcinoma but the incidence of adenocarcinoma is rising rapidly. Adenocarcinoma is now the most common type of oesophageal cancer and is more likely to develop in patients with a history of gastro-oesophageal reflux disease (GORD) or Barrett's.

The majority of tumours are in the middle third of the oesophagus.

#### Risk factors

- smoking
- alcohol
- GORD
- Barrett's oesophagus
- achalasia
- Plummer-Vinson syndrome
- rare: coeliac disease, scleroderma



A 23-year-old man is investigated for chronic diarrhoea associated with raised inflammatory markers. A bowel biopsy is taken. Which one of the following findings is most suggestive of ulcerative colitis?

- ☐ A. Multiple granulomas
- ☐ B. Goblet cell depletion
- ☐ C. Inflammation affecting the serosa
- ☐ D. Cobblestone appearance
- ☐ E. Skip lesions

[Next question](#)

### Inflammatory bowel disease: key differences

The two main types of inflammatory bowel disease are Crohn's disease and Ulcerative colitis. They have many similarities in terms of presenting symptoms, investigation findings and management options. There are however some key differences which are highlighted in table below:

	Crohn's disease (CD)	Ulcerative colitis (UC)
<b>Features</b>	Diarrhoea usually non-bloody Weight loss more prominent Upper gastrointestinal symptoms, mouth ulcers, perianal disease Abdominal mass palpable in the right iliac fossa	Bloody diarrhoea more common Abdominal pain in the left lower quadrant Tenesmus
<b>Extra-intestinal</b>		Primary sclerosing cholangitis more common
<b>Complications</b>	Obstruction, fistula, colorectal cancer	Risk of colorectal cancer high in UC than CD
<b>Pathology</b>	Lesions may be seen anywhere from the mouth to anus  Skip lesions may be present	Inflammation always starts at rectum and never spreads beyond ileocaecal valve  Continuous disease
<b>Histology</b>	Inflammation in all layers from mucosa to serosa  <ul style="list-style-type: none"> <li>increased goblet cells</li> <li>granulomas</li> </ul>	No inflammation beyond submucosa (unless fulminant disease) - inflammatory cell infiltrate in lamina propria  <ul style="list-style-type: none"> <li>neutrophils migrate through the walls of glands to form crypt abscesses</li> <li>depletion of goblet cells and mucin from gland epithelium</li> </ul>

		<ul style="list-style-type: none"> <li>granulomas are infrequent</li> </ul>
<b>Endoscopy</b>	Deep ulcers, skip lesions - 'cobble-stone' appearance	Widespread ulceration with preservation of adjacent mucosa which has the appearance of polyps ('pseudopolyps')
<b>Radiology</b>	<p>Small bowel enema</p> <ul style="list-style-type: none"> <li>high sensitivity and specificity for examination of the terminal ileum</li> <li>strictures: 'Kantor's string sign'</li> <li>proximal bowel dilation</li> <li>'rose thorn' ulcers</li> <li>fistulae</li> </ul>	<p>Barium enema</p> <ul style="list-style-type: none"> <li>loss of haustrations</li> <li>superficial ulceration, 'pseudopolyps'</li> <li>long standing disease: colon is narrow and short - 'drainpipe colon'</li> </ul>

Which one of the following is not a feature of Peutz-Jeghers syndrome?

<input type="radio"/>	A. Intestinal obstruction
<input type="radio"/>	B. Pigmented lesions on palms
<input type="radio"/>	C. More than 10-fold increased risk of gastrointestinal malignancy
<input type="radio"/>	D. Osteomas
<input type="radio"/>	E. Iron-deficiency anaemia

Next question

Osteomas are a feature of Gardner's syndrome, a variant of familial adenomatous polyposis

### Peutz-Jeghers syndrome

Peutz-Jeghers syndrome is an autosomal dominant condition characterised by numerous hamartomatous polyps in the gastrointestinal tract. It is also associated with pigmented freckles on the lips, face, palms and soles. Around 50% of patients will have died from a gastrointestinal tract cancer by the age of 60 years.

#### Genetics

- autosomal dominant
- responsible gene encodes serine threonine kinase LKB1 or STK11

#### Features

- hamartomatous polyps in GI tract (mainly small bowel)
- pigmented lesions on lips, oral mucosa, face, palms and soles
- intestinal obstruction e.g. intussusception
- gastrointestinal bleeding

#### Management

- conservative unless complications develop

### Question 145 of 151

Next

A 29-year-old woman who is 30 weeks pregnant is admitted to the Emergency Department with central abdominal pain. Initial blood tests show the following:

Amylase	1,438 u/dl
---------	------------

What is the most likely cause of this presentation?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Gestational diabetes                       |
| <input type="radio"/> | B. HELLP syndrome                             |
| <input type="radio"/> | C. Gallstones                                 |
| <input type="radio"/> | D. Hypertriglyceridaemia-induced pancreatitis |
| <input type="radio"/> | E. Pre-eclampsia                              |

Next question

Pancreatitis occurs in around 1 in 2,000 pregnancies. Most cases of pancreatitis in pregnancy are gallstone related.

#### Acute pancreatitis: causes

The vast majority of cases in the UK are caused by gallstones and alcohol

Popular mnemonic is **GET SMASHED**

- **G**allstones
- **E**thanol
- **T**rauma
- **S**teroids
- **M**umps (other viruses include Coxsackie B)
- **A**utoimmune (e.g. polyarteritis nodosa), **A**scaris infection
- **S**corpion venom
- **H**ypertriglyceridaemia, **H**yperchylomicronaemia, **H**ypercalcaemia, **H**ypothermia
- **E**RCP
- **D**rugs (azathioprine, mesalazine\*, didanosine, bendroflumethiazide, furosemide, pentamidine, steroids, sodium valproate)

\*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

A 27-year-old female presents with alternating loose and hard stools associated with abdominal discomfort and bloating. Which one of the following is it most important to do before making a positive diagnosis of irritable bowel syndrome?

<input type="radio"/>	A. Arrange ultrasound abdomen
<input type="radio"/>	B. Flexible sigmoidoscopy
<input type="radio"/>	C. Ask about family history of ovarian cancer
<input type="radio"/>	D. Use a standardised screening tool for depression
<input type="radio"/>	E. Perform thyroid function tests

### Irritable bowel syndrome: diagnosis

NICE published clinical guidelines on the diagnosis and management of irritable bowel syndrome (IBS) in 2008

The diagnosis of IBS should be considered if the patient has had the following for at least 6 months:

- abdominal pain, and/or
- bloating, and/or
- change in bowel habit

A positive diagnosis of IBS should be made if the patient has abdominal pain relieved by defecation or associated with altered bowel frequency stool form, in addition to 2 of the following 4 symptoms:

- altered stool passage (straining, urgency, incomplete evacuation)
- abdominal bloating (more common in women than men), distension, tension or hardness
- symptoms made worse by eating
- passage of mucus

Features such as lethargy, nausea, backache and bladder symptoms may also support the diagnosis

Red flag features should be enquired about:

- rectal bleeding
- unexplained/unintentional weight loss
- family history of bowel or ovarian cancer
- onset after 60 years of age

Suggested primary care investigations are:

- full blood count
- ESR/CRP
- coeliac disease screen (tissue transglutaminase antibodies)

Which one of the following adverse effects is least associated with sulfasalazine?

<input type="radio"/>	A. Male infertility
<input type="radio"/>	B. Skin rashes
<input type="radio"/>	C. Visual disturbance
<input type="radio"/>	D. Diarrhoea
<input type="radio"/>	E. Agranulocytosis

Next question

### Aminosalicylate drugs

5-aminosalicylic acid (5-ASA) is released in the colon and is not absorbed. It acts locally as an anti-inflammatory. The mechanism of action is not fully understood but 5-ASA may inhibit prostaglandin synthesis

#### Sulphasalazine

- a combination of sulphapyridine (a sulphonamide) and 5-ASA
- many side-effects are due to the sulphapyridine moiety: rashes, oligospermia, headache, Heinz body anaemia
- other side-effects are common to 5-ASA drugs (see mesalazine)

#### Mesalazine

- a delayed release form of 5-ASA
- sulphapyridine side-effects seen in patients taking sulphasalazine are avoided
- mesalazine is still however associated with side-effects such as GI upset, headache, agranulocytosis, pancreatitis\*, interstitial nephritis

#### Olsalazine

- two molecules of 5-ASA linked by a diazo bond, which is broken by colonic bacteria

\*pancreatitis is 7 times more common in patients taking mesalazine than sulfasalazine

Which one of the following is not a contraindication to performing a percutaneous liver biopsy?

<input type="radio"/>	A. INR 2.6
<input type="radio"/>	B. Viral hepatitis
<input type="radio"/>	C. Hydatid cyst
<input type="radio"/>	D. Uncooperative patient
<input type="radio"/>	E. Haemoangioma

Next question

## Liver biopsy

Contraindications to percutaneous liver biopsy

- deranged clotting (e.g. INR > 1.4)
- low platelets (e.g. <  $60 \times 10^9/l$ )
- anaemia
- bile duct obstruction
- hydatid cyst
- haemoangioma
- uncooperative patient
- ascites

Which one of the following factors is most responsible for the increased rate of colorectal cancer in patients with ulcerative colitis?

<input type="radio"/>	A. Shared mutation in the HNPCC gene
<input checked="" type="radio"/>	B. Chronic inflammation
<input type="radio"/>	C. Increased surveillance with colonoscopy
<input type="radio"/>	D. Increased susceptibility to bacterial gastroenteritis
<input type="radio"/>	E. Prolonged immunosuppression

[Next question](#)

Chronic inflammation is an important factor in the development of a number of cancers. An example is hepatocellular carcinoma secondary to viral hepatitis.

### Ulcerative colitis: colorectal cancer

#### Overview

- risk of colorectal cancer is 10-20 times that of general population
- the increased risk is mainly related to chronic inflammation
- worse prognosis than patients without ulcerative colitis (partly due to delayed diagnosis)
- lesions may be multifocal

#### Factors increasing risk of cancer

- disease duration > 10 years
- patients with pancolitis
- onset before 15 years old
- unremitting disease
- poor compliance to treatment



Which one of the following is least associated with Crohn's disease?

<input type="radio"/>	A. Fistulae
<input type="radio"/>	B. Kantor's string sign
<input type="radio"/>	C. 'Cobblestone' pattern of mucosa
<input type="radio"/>	D. Crypt abscesses
<input type="radio"/>	E. Involvement of all layers of bowel wall

Next question

Crypt abscesses are sometimes seen in Crohn's disease but they are more commonly associated with ulcerative colitis

### Crohn's disease: investigation

Crohn's disease is a form of inflammatory bowel disease. It commonly affects the terminal ileum and colon but may be seen anywhere from the mouth to anus

#### Bloods

- C-reactive protein correlates well with disease activity

#### Endoscopy

- colonoscopy is the investigation of choice
- features suggest of Crohn's include deep ulcers, skip lesions

#### Histology

- inflammation in all layers from mucosa to serosa
- goblet cells
- granulomas

#### Small bowel enema

- high sensitivity and specificity for examination of the terminal ileum
- strictures: 'Kantor's string sign'
- proximal bowel dilation
- 'rose thorn' ulcers
- fistulae

### Question 151 of 151

What are the most common type of antibodies seen in pernicious anaemia?

<input type="radio"/>	A. Vitamin B12 receptor antibodies
<input type="radio"/>	B. Gastric parietal cell antibodies
<input type="radio"/>	C. Jejunal mucosa antibodies
<input type="radio"/>	D. Intrinsic factor antibodies
<input type="radio"/>	E. Vitamin B12 antibodies

### Pernicious anaemia: investigation

#### Investigation

- anti gastric parietal cell antibodies in 90% (but low specificity)
- anti intrinsic factor antibodies in 50% (specific for pernicious anaemia)
- macrocytic anaemia
- low WCC and platelets
- LDH may be raised due to ineffective erythropoiesis
- also low serum B12, hypersegmented polymorphs on film, megaloblasts in marrow
- Schilling test

#### Schilling test

- radiolabelled B12 given on two occasions
- first on its own
- second with oral IF
- urine B12 levels measured

Which one of the following is a recognised cause of hypokalaemia associated with hypertension

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Liddle's syndrome      |
| <input type="radio"/> | B. Bartter's syndrome     |
| <input type="radio"/> | C. Gitelman syndrome      |
| <input type="radio"/> | D. Ciclosporin            |
| <input type="radio"/> | E. Renal tubular acidosis |

Next question

Liddle's syndrome: hypokalaemia + hypertension

Liddle's syndrome is an autosomal dominant disorder that mimics hyperaldosteronism, resulting in hypokalaemia associated with hypertension.

Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the  $\text{Na}^+ \text{K}^+ 2\text{Cl}^-$  cotransporter in the ascending loop of Henle. It should be noted that it is associated with normotension.

Gitelman's syndrome is due to a defect in the thiazide-sensitive  $\text{Na}^+ \text{Cl}^-$  transporter in the distal convoluted tubule. It is associated with hypokalaemia and normotension.

### Hypokalaemia and hypertension

For exams it is useful to be able to classify the causes of hypokalaemia in to those associated with hypertension, and those which are not

Hypokalaemia with hypertension

- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)
- Liddle's syndrome
- 11-beta hydroxylase deficiency\*

Carbenoxolone, an anti-ulcer drug, and liquorice excess can potentially cause hypokalaemia associated with hypertension

Hypokalaemia without hypertension

- diuretics
- GI loss (e.g. Diarrhoea, vomiting)

- renal tubular acidosis (type 1 and 2\*\*)
- Bartter's syndrome
- Gitelman syndrome

\*21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

\*\*type 4 renal tubular acidosis is associated with hyperkalaemia

**Question 2 of 153**

Next

A 15-year-old girl is investigated for primary amenorrhoea, despite having developed secondary sexual characteristics at 11 years of age. On examination she has well developed breasts with scanty pubic hair and small bilateral groin swellings. What is the most likely diagnosis?

<input type="radio"/>	A. Congenital adrenal hyperplasia
<input type="radio"/>	B. Polycystic ovarian syndrome
<input type="radio"/>	C. Turner's syndrome
<input checked="" type="radio"/>	D. Complete androgen insensitivity syndrome
<input type="radio"/>	E. Mullerian duct agenesis

Next question

**Androgen insensitivity syndrome**

Androgen insensitivity syndrome is an X-linked recessive condition due to end-organ resistance to testosterone causing genotypically male children (46XY) to have a female phenotype. Complete androgen insensitivity syndrome is the new term for testicular feminisation syndrome

**Features**

- 'primary amenorrhoea'
- undescended testes causing groin swellings
- breast development may occur as a result of conversion of testosterone to oestradiol

**Diagnosis**

- buccal smear or chromosomal analysis to reveal 46XY genotype

**Management**

- counselling - raise child as female
- bilateral orchidectomy (increased risk of testicular cancer due to undescended testes)
- oestrogen therapy

**Question 3 of 153**

Next

A 33-year-old woman presents with weight loss and excessive sweating. her partner reports that she is 'on edge' all the time and during the consultation you notice a fine tremor. Her pulse rate is 96/min. A large, non-tender goitre is noted. Examination of her eyes is unremarkable with no evidence of exophthalmos.

Free T4	26 pmol/l
Free T3	12.2 pmol/l (3.0-7.5)
TSH	< 0.05 mu/l

What is the most likely diagnosis?

- ☐ A. Toxic multinodular goitre
- ☐ B. Hashimoto's thyroiditis
- ☐ C. T3-secreting adenoma
- ☐ D. De Quervain's thyroiditis
- ☐ E. Graves' disease

Next question

Graves' disease is the most common cause of thyrotoxicosis

Only around 30% of patients with Graves' disease have eye disease so the absence of eye signs does not exclude the diagnosis.

**Graves' disease: features**

Graves' disease is the most common cause of thyrotoxicosis. It is typically seen in women aged 30-50 years.

**Features**

- typical features of thyrotoxicosis
- specific signs limited to Grave's (see below)

**Features seen in Graves' but not in other causes of thyrotoxicosis**

- eye signs (30% of patients): exophthalmos, ophthalmoplegia
- pretibial myxoedema
- thyroid acropachy

**Autoantibodies**

- anti-TSH receptor stimulating antibodies (90%)
- anti-thyroid peroxidase antibodies (50%)

**Question 4 of 153**

Next

A 46-year-old man with suspected diabetes mellitus has an oral glucose tolerance test, following the standard WHO protocol. The following results are obtained:

Time (hours)	Blood glucose (mmol/l)
0	5.7
2	7.6

How should these results be interpreted?

- ☐ A. Normal
- ☐ B. Impaired fasting glucose and impaired glucose tolerance
- ☐ C. Diabetes mellitus
- ☐ D. Impaired glucose tolerance
- ☐ E. Impaired fasting glucose

Next question

Both the fasting and two-hour glucose are within normal limits.

**Diabetes mellitus: diagnosis**

The following is based on the World Health Organisation (WHO) 2006 guidelines.

**Diabetes mellitus**

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

In 2011 WHO released supplementary guidance on the use of HbA1c on the diagnosis of diabetes:

- a HbA1c of greater than or equal to 6.5% (48 mmol/mol) is diagnostic of diabetes mellitus
- a HbA1c value of less than 6.5% does not exclude diabetes (i.e. it is not as sensitive as fasting samples for detecting diabetes)
- in patients without symptoms, the test must be repeated to confirm the diagnosis
- it should be remembered that misleading HbA1c results can be caused by increased red cell turnover (for example anaemia, haemoglobinopathies and pregnancy)

## **Impaired fasting glucose and impaired glucose tolerance**

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'



**Question 5 of 153**

Next

A 45-year-old man is referred to the acute medical unit. He had presented earlier in the day to the GP complaining of ongoing fatigue and polydipsia. A BM (finger-prick glucose) taken in the surgery was 22.3 mmol/l. On examination he is an obese man (BMI 36kg/m<sup>2</sup>) with a pulse of 84 bpm and blood pressure of 144/84 mmHg. Blood tests reveal the following:

Na <sup>+</sup>	140 mmol/l
K <sup>+</sup>	3.9 mmol/l
Bicarbonate	23 mmol/l
Urea	5.2 mmol/l
Creatinine	101 µmol/l
Glucose	21.2 mmol/l

What is the most appropriate initial management?

<input type="radio"/>	A. Gliclazide
<input type="radio"/>	B. Pioglitazone
<input type="radio"/>	C. Weight loss
<input checked="" type="radio"/>	D. Metformin
<input type="radio"/>	E. Commence insulin therapy

Next question

Weight reduction alone would be insufficient in this patient with frank diabetes

**Metformin**

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

**Mechanism of action**

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

**Adverse effects**

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem

- lactic acidosis\* with severe liver disease or renal failure

#### Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is  $> 130 \mu\text{mol/l}$  and stopping metformin if  $> 150 \mu\text{mol/l}$
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

A 35-year-old female who has recently being diagnosed with Grave's disease presents for review 3 months after starting a 'block and replace' regime with carbimazole and thyroxine. She is concerned about developing thyroid eye disease. What is the best way that her risk of developing thyroid eye disease can be reduced?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. Reduce alcohol intake              |
| <input type="radio"/> | B. A diet rich in omega-3 fatty acids |
| <input type="radio"/> | C. Regular exercise                   |
| <input type="radio"/> | D. Stop smoking                       |
| <input type="radio"/> | E. Lose weight                        |

[Next question](#)

Smoking is the most important modifiable risk factor for the development of thyroid eye disease

### Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

#### Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

#### Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

#### Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

**Question 7 of 153**

Next

A 3-year-old boy is investigated for lethargy. Examination is unremarkable with a blood pressure of 90/46 mmHg (normal for his age). Blood tests reveal:

Na <sup>+</sup>	140 mmol/l
K <sup>+</sup>	2.6 mmol/l
Bicarbonate	33 mmol/l
Urea	4.2 mmol/l
Creatinine	91 µmol/l

Which one of the following conditions is most likely to be responsible?

- ☐ A. Cushing's syndrome
- ☐ B. Conn's syndrome
- ☐ C. 11-beta hydroxylase deficiency
- ☐ D. Bartter's syndrome
- ☐ E. Liddle's syndrome

Next question

Bartter's syndrome is associated with normotension

Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the Na<sup>+</sup> K<sup>+</sup> 2Cl<sup>-</sup> cotransporter in the ascending loop of Henle

**Hypokalaemia and hypertension**

For exams it is useful to be able to classify the causes of hypokalaemia in to those associated with hypertension, and those which are not

Hypokalaemia with hypertension

- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)
- Liddle's syndrome
- 11-beta hydroxylase deficiency\*

Carbenoxolone, an anti-ulcer drug, and liquorice excess can potentially cause hypokalaemia associated with hypertension

Hypokalaemia without hypertension

- diuretics
- GI loss (e.g. Diarrhoea, vomiting)
- renal tubular acidosis (type 1 and 2\*\*)
- Bartter's syndrome
- Gitelman syndrome

\*21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

\*\*type 4 renal tubular acidosis is associated with hyperkalaemia

**Question 8 of 153**

Next

A 45-year-old man is investigated following referral to the endocrinology clinic with polydipsia. Plasma glucose and calcium are normal. A water deprivation test is performed with the following results:

Starting plasma osm.	319 mOsmol/l (275-295 mOsmol/l)
Final urine osm.	142 mOsmol/l
Urine osm. post-DDAVP	885 mOsmol/l

What is the most likely diagnosis?

<input type="radio"/>	A. Psychogenic polydipsia
<input type="radio"/>	B. Nephrogenic diabetes insipidus
<input type="radio"/>	C. Primary hyperparathyroidism
<input type="radio"/>	D. Pseudohypoparathyroidism
<input type="radio"/>	E. Cranial diabetes insipidus

Next question

A dramatic improvement is seen in the ability of the kidneys to concentrate urine following the administration of DDAVP. This points towards a diagnosis of cranial diabetes insipidus

**Water deprivation test**

Method

- prevent patient drinking water
- ask patient to empty bladder
- hourly urine and plasma osmolalities

	Starting plasma osm.	Final urine osm.	Urine osm. post-DDAVP
<b>Normal</b>	Normal	> 600	> 600
<b>Psychogenic polydipsia</b>	Low	> 400	> 400
<b>Cranial DI</b>	High	< 300	> 600
<b>Nephrogenic DI</b>	High	< 300	< 300

A 78-year-old nursing home resident is admitted to the acute medical unit after being found collapsed in his room. A carer from the nursing home is present and reports that he has had regular 'hypos' recently. On admission he was drowsy and the blood glucose was 1.8 mmol/l. Following intravenous dextrose the patient's condition significantly improved.

His medication on admission is as follows:

Metformin 1g bd  
Gliclazide 160mg od  
Pioglitazone 45mg od  
Aspirin 75mg od  
Simvastatin 40mg on

What is the most appropriate initial action?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Stop metformin                         |
| <input type="radio"/> | B. Stop pioglitazone                      |
| <input type="radio"/> | C. Stop gliclazide                        |
| <input type="radio"/> | D. Make no changes to the medication      |
| <input type="radio"/> | E. Stop all oral antidiabetic medications |

Next question

Neither metformin nor pioglitazone cause hypoglycaemia. The gliclazide dose is therefore responsible and should be stopped whilst deciding upon longer term changes to his medication.

### Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

#### Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

HbA1c

- the general target for patients is 48 mmol/mol (DCCT = 6.5%). HbA1c levels below 48 mmol/mol (DCCT = 6.5%) should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

#### Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first\*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 48 mmol/mol (DCCT = 6.5%)
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 58 mmol/mol (DCCT = 7.5%) then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% at 6 months)

#### Starting insulin

- usually commenced if HbA1c > 58 mmol/mol (DCCT = 7.5%)
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

#### Other risk factor modification

- current NICE guidelines suggest giving aspirin to all patients > 50 years and to younger patients with other significant risk factors. However, recent evidence does not support this approach. The 2010 SIGN guidelines do not advocate the use of aspirin for primary prevention in diabetics
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reached consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

\*many local protocols now recommend starting metformin upon diagnosis



**Question 10 of 153**[Next](#)

A 45-year-old female is admitted to the Emergency Department with abdominal pain associated with vomiting. She has a past medical history of hypothyroidism and takes thyroxine. On examination she is pyrexial at 37.6°C. Pulse is 110 bpm with a blood pressure of 100/64 mmHg. Blood results show the following:

Na <sup>+</sup>	131 mmol/l
K <sup>+</sup>	4.9 mmol/l
Urea	8.1 mmol/l
Creatinine	110 µmol/l
Glucose	3.3 mmol/l

What treatment should be given first?

<input type="radio"/>	A. Ceftriaxone + benzylpenicillin
<input type="radio"/>	B. Glucagon
<input type="radio"/>	C. Propranolol
<input type="radio"/>	D. Triiodothyronine
<input type="radio"/>	E. Hydrocortisone

[Next question](#)

This is a typical history of Addison's. Patients may have a history of other autoimmune conditions such as thyroid disorders. Steroids should be given as soon as possible

**Addison's disease**

Autoimmune destruction of the adrenal glands is the commonest cause of hypoadrenalism in the UK, accounting for 80% of cases

**Features**

- lethargy, weakness, anorexia, nausea & vomiting, weight loss
- hyperpigmentation, vitiligo, loss of pubic hair in women
- crisis: collapse, shock, pyrexia

**Other causes of hypoadrenalism****Primary causes**

- tuberculosis
- metastases (e.g. bronchial carcinoma)
- meningococcal septicaemia (Waterhouse-Friderichsen syndrome)

- HIV
- antiphospholipid syndrome

#### Secondary causes

- pituitary disorders (e.g. tumours, irradiation, infiltration)

#### Exogenous glucocorticoid therapy

A 56-year-old man is reviewed in the Cardiology outpatient clinic following a myocardial infarction one year previously. During his admission he was found to be hypertensive and diabetic. He complains that he has put on 5kg in weight in the past 6 months. Which of his medications may be contributing to his weight gain?

<input type="radio"/>	A. Metformin
<input type="radio"/>	B. Losartan
<input type="radio"/>	C. Clopidogrel
<input type="radio"/>	D. Gliclazide
<input type="radio"/>	E. Simvastatin

[Next question](#)

## Sulfonylureas

Sulfonylureas are oral hypoglycaemic drugs used in the management of type 2 diabetes mellitus. They work by increasing pancreatic insulin secretion and hence are only effective if functional B-cells are present.

### Common adverse effects

- hypoglycaemic episodes (more common with long acting preparations such as chlorpropamide)
- weight gain

### Rarer adverse effects

- syndrome of inappropriate ADH secretion
- bone marrow suppression
- liver damage (cholestatic)
- photosensitivity
- peripheral neuropathy

Sulfonylureas should be avoided in breast feeding and pregnancy

**Question 12 of 153**

Next

A 48-year-old man who was diagnosed with type 2 diabetes mellitus presents for review. During his annual review he was noted to have the following results:

Total cholesterol	5.3 mmol/l
HDL cholesterol	1.0 mmol/l
LDL cholesterol	3.1 mmol/l
Triglyceride	1.7 mmol/l
HbA1c	6.4%

His current medication is metformin 500mg tds. According to recent NICE guidelines, what is the most appropriate action?

- ☐ A. Simvastatin 40mg on
- ☐ B. Lifestyle advice, repeat lipid profile in 3 months
- ☐ C. Nicotinic acid
- ☐ D. Atorvastatin 40mg on
- ☐ E. Increase his metformin slowly to 1g tds

Next question

Patients over the age of 40 years with type 2 diabetes mellitus should be started on a statin if they have any other risk factors for cardiovascular disease, such as smoking, hypertension or a 'high-risk' lipid profile. This patient has a high-risk lipid profile and should therefore be offered statin therapy.

A high-risk lipid profile may be defined as:

- total cholesterol > 4.0 mmol/L, or
- low-density lipoprotein cholesterol > 2.0 mmol/L, or
- triglycerides > 4.5 mmol/L

Please see the CKS link for more details.

**Hyperlipidaemia: management**

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

**Primary prevention**

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

NICE updated their lipid guidelines so that the following risk models are valid:

- Framingham
- Joint British Society 2 (JBS2)
- QRISK
- ASSIGN (Scotland only)

The 1991 Framingham equations may still be used. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- males of South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

## **Secondary prevention**

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing simvastatin to 80mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained.

**Question 13 of 153**

Next

A 35-year-old man is investigated for lethargy, arthralgia and deranged liver function tests. He is eventually diagnosed as having hereditary hemochromatosis. His wife has a genetic test which shows she is not a carrier of the disease. What is the chance his child will develop haemochromatosis?

<input type="radio"/>	A. 0%
<input type="radio"/>	B. 25%
<input type="radio"/>	C. 50% if female, 0% if male
<input type="radio"/>	D. 50% if male, 0% if female
<input type="radio"/>	E. 50%

Next question

Haemochromatosis is an autosomal recessive condition. If one of the parents has haemochromatosis (i.e. is homozygous) and the other is not a carrier/affected then all the children will inherit one copy of the gene from the affected parent and hence will be carriers.

**Haemochromatosis: features**

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6\*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

**Epidemiology**

- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

**Presenting features**

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	Irreversible complications
--------------------------	----------------------------

- Cardiomyopathy
- Skin pigmentation

- Liver cirrhosis\*\*
- Diabetes mellitus
- Hypogonadotrophic hypogonadism
- Arthropathy

\*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

\*\*whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

A 61-year-old man presents as he developed enlargement of his breast tissue. He has become very self-conscious and is worried about going on holiday in the summer. Which one of the following drugs is most likely to be responsible?

<input type="radio"/>	A. Amitriptyline
<input type="radio"/>	B. Isoniazid
<input type="radio"/>	C. Verapamil
<input type="radio"/>	D. Methyldopa
<input type="radio"/>	E. Spironolactone

[Next question](#)

All the above drugs may cause gynaecomastia but spironolactone is the most common cause.

### Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

#### Causes of gynaecomastia

- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below

#### Drug causes of gynaecomastia

- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- gonadorelin analogues e.g. Goserelin, buserelin
- oestrogens, anabolic steroids



Very rare drug causes of gynaecomastia

- tricyclics
- isoniazid
- calcium channel blockers
- heroin
- busulfan
- methyldopa

A 53 year man presents as his wife has noticed a change in his appearance. He has also noticed his hands seem larger. On examination blood pressure is 170/94 and he is noted to have bitemporal hemianopia. What is the most appropriate first-line treatment?

<input type="radio"/>	A. Octreotide
<input type="radio"/>	B. External irradiation
<input type="radio"/>	C. Pegvisomant
<input type="radio"/>	D. Trans-sphenoidal surgery
<input type="radio"/>	E. Bromocriptine

[Next question](#)

Trans-sphenoidal surgery is the treatment of choice in acromegaly. There is no significant evidence base supporting the use of pre-operative octreotide

### Acromegaly: management

Trans-sphenoidal surgery is first-line treatment for acromegaly in the majority of patients

Dopamine agonists

- for example bromocriptine
- the first effective medical treatment for acromegaly, however now superseded by somatostatin analogues
- effective only in a minority of patients

Somatostatin analogue

- for example octreotide
- effective in 50-70% of patients
- may be used as an adjunct to surgery

Pegvisomant

- GH receptor antagonist - prevents dimerization of the GH receptor
- once daily s/c administration
- very effective - decreases IGF-1 levels in 90% of patients to normal
- doesn't reduce tumour volume therefore surgery still needed if mass effect

External irradiation is sometimes used for older patients or following failed surgical/medical treatment

A 43-year-old man is admitted to hospital with pneumonia. His past medical history includes Addison's disease for which he takes hydrocortisone (20mg in the mornings and 10mg in the afternoon). What is the most appropriate action with respect to his steroid dose?

- ☐ A. Continue to take the same dose
- ☐ B. Double hydrocortisone to 40mg mornings and 20mg afternoon
- ☐ C. Halve hydrocortisone to 10mg mornings and 5mg afternoon
- ☐ D. Continue to take the same dose + prescribe a proton pump inhibitor
- ☐ E. Continue the same morning dose + stop the afternoon dose

Next question

Patients on long-term steroids should have their doses doubled during intercurrent illness

## Corticosteroids

Corticosteroids are amongst the most commonly prescribed therapies in clinical practice. They are used both systemically (oral or intravenous) or locally (skin creams, inhalers, eye drops, intra-articular). They augment and in some cases replace the natural glucocorticoid and mineralocorticoid activity of endogenous steroids.

The relative glucocorticoid and mineralocorticoid activity of commonly used steroids is shown below:

Minimal glucocorticoid activity, very high mineralocorticoid activity,	Glucocorticoid activity, high mineralocorticoid activity,	Predominant glucocorticoid activity, low mineralocorticoid activity	Very high glucocorticoid activity, minimal mineralocorticoid activity
Fludrocortisone	Hydrocortisone	Prednisolone	Dexamethasone Betmethasone

## Side-effects

The side-effects of corticosteroids are numerous and represent the single greatest limitation on their usage. Side-effects are more common with systemic and prolonged therapy.

### Glucocorticoid side-effects

- endocrine: impaired glucose regulation, increased appetite/weight gain, hirsutism, hyperlipidaemia
- Cushing's syndrome: moon face, buffalo hump, striae
- musculoskeletal: osteoporosis, proximal myopathy, avascular necrosis of the femoral head

- immunosuppression: increased susceptibility to severe infection, reactivation of tuberculosis
- psychiatric: insomnia, mania, depression
- gastrointestinal: peptic ulceration, acute pancreatitis
- ophthalmic: glaucoma, cataracts
- suppression of growth in children

#### Mineralocorticoid side-effects

- fluid retention
- hypertension

#### Selected points on the use of corticosteroids:

- patients on long-term steroids should have their doses doubled during intercurrent illness
- the BNF suggests gradual withdrawal of systemic corticosteroids if patients have: received more than 40mg prednisolone daily for more than one week, received more than 3 weeks treatment or recently received repeated courses

What causes increased sweating in patients with acromegaly?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Increased sodium content in sweat |
| <input type="radio"/> | B. Raised basal metabolic rate       |
| <input type="radio"/> | C. Episodic hypoglycaemia            |
| <input type="radio"/> | D. Low-grade chronic pyrexia         |
| <input type="radio"/> | E. Sweat gland hypertrophy           |

Next question

Acromegaly: increased sweating is caused by sweat gland hypertrophy

### Acromegaly: features

In acromegaly there is excess growth hormone secondary to a pituitary adenoma in over 95% of cases. A minority of cases are caused by ectopic GHRH or GH production by tumours e.g. pancreatic

#### Features

- coarse facial appearance, spade-like hands, increase in shoe size
- large tongue, prognathism, interdental spaces
- excessive sweating and oily skin
- features of pituitary tumour: hypopituitarism, headaches, bitemporal hemianopia
- raised prolactin in 1/3 of cases --> galactorrhoea
- 6% of patients have MEN-1

#### Complications

- hypertension
- diabetes (>10%)
- cardiomyopathy
- colorectal cancer

**Question 18 of 153**

Next

A 46-year-old woman is referred to endocrine with a tender neck swelling. Blood results are as follows:

TSH	<0.1 mU/l
T4	188 nmol/l
Hb	14.2 g/dl
Plt	$377 \times 10^9/l$
WBC	$6.4 \times 10^9/l$
ESR	65 mm/hr

Technetium thyroid scan shows decreased uptake globally

What is the most likely diagnosis?

<input type="radio"/>	A. Sick thyroid syndrome
<input type="radio"/>	B. Acute bacterial thyroiditis
<input type="radio"/>	C. Hashimoto's thyroiditis
<input type="radio"/>	D. Subacute thyroiditis
<input type="radio"/>	E. Toxic multinodular goitre

Next question

Subacute thyroiditis is suggested by the tender goitre, hyperthyroidism and raised ESR. The globally reduced uptake on technetium thyroid scan is also typical

**Subacute (De Quervain's) thyroiditis**

Subacute thyroiditis (also known as De Quervain's thyroiditis) is thought to occur following viral infection and typically presents with hyperthyroidism

Features

- hyperthyroidism
- painful goitre
- raised ESR
- globally reduced uptake on iodine-131 scan

Management

- usually self-limiting - most patients do not require treatment
- thyroid pain may respond to aspirin or other NSAIDs
- in more severe cases steroids are used, particularly if hypothyroidism develops

**Question 19 of 153**

Next

A 68-year-old woman is found to have the following blood tests:

TSH	0.05 mu/l
Free T4	19 pmol/l (range 9-25 pmol/l)
Free T3	7 pmol/l (range 3-9 pmol/l)

If left untreated, what are the most likely possible consequences?

<input type="radio"/>	A. Supraventricular arrhythmias and osteoporosis
<input type="radio"/>	B. Supraventricular arrhythmias and hyperlipidaemia
<input type="radio"/>	C. Hypothyroidism and impaired glucose tolerance
<input type="radio"/>	D. Myasthenia gravis and hypothyroidism
<input type="radio"/>	E. Impaired glucose tolerance and hyperlipidaemia

Next question

**Subclinical hyperthyroidism**

Subclinical hyperthyroidism is an entity which is gaining increasing recognition. It is defined as:

- normal serum free thyroxine and triiodothyronine levels
- with a thyroid stimulating hormone (TSH) below normal range (usually < 0.1 mu/l)

Causes

- multinodular goitre, particularly in elderly females
- excessive thyroxine may give a similar biochemical picture

The importance in recognising subclinical hyperthyroidism lies in the potential effect on the cardiovascular system (atrial fibrillation) and bone metabolism (osteoporosis). It may also impact on quality of life and increase the likelihood of dementia

Management

- TSH levels often revert to normal - therefore levels must be persistently low to warrant intervention
- a reasonable treatment option is a therapeutic trial of low-dose antithyroid agents for approximately 6 months in an effort to induce a remission

Which one of the following statements regarding maturity-onset diabetes of the young (MODY) is true?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. There is usually a strong family history               |
| <input type="radio"/> | B. Body mass index is typically > 30                      |
| <input type="radio"/> | C. Doesn't respond to glimepiride                         |
| <input type="radio"/> | D. Autosomal recessive inheritance                        |
| <input type="radio"/> | E. Frequent episodes of diabetic ketoacidosis are typical |

Next question

## MODY

Maturity-onset diabetes of the young (MODY) is characterised by the development of type 2 diabetes mellitus in patients < 25 years old. It is typically inherited as an autosomal dominant condition. Over six different genetic mutations have so far been identified as leading to MODY. Ketosis is not a feature at presentation

### MODY 3

- 60% of cases
- due to a defect in the HNF-1 alpha gene

### MODY 2

- 20% of cases
- due to a defect in the glucokinase gene



A 45-year-old woman is investigated for weight gain. She had had been unwell for around four months and described a combination of symptoms including depression, facial male-pattern hair growth and reduced libido. During the work-up she was found to be hypertensive with a blood pressure of 170/100 mmHg. Which one of the following tests is most likely to be diagnostic?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Renin:aldosterone levels                 |
| <input type="radio"/> | B. High-dose dexamethasone suppression test |
| <input type="radio"/> | C. Pelvic ultrasound                        |
| <input type="radio"/> | D. Overnight dexamethasone suppression test |
| <input type="radio"/> | E. 24 hr urinary free cortisol              |

[Next question](#)

The overnight dexamethasone suppression test is the best test to diagnosis Cushing's syndrome

This patient has Cushing's syndrome as evidenced by the weight gain, hirsutism, depression and hypertension. Polycystic ovarian syndrome may give some of these features but would not cause such an elevated blood pressure.

### Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

### Tests to confirm Cushing's syndrome

The two most commonly used tests are:

- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

### Localisation tests

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test

- if pituitary source then cortisol suppressed

- if ectopic/adrenal then no change in cortisol

#### CRH stimulation

- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

**Question 22 of 153**

Next

A 36-year-old woman presents with feeling tired and cold all the time. On examination a firm, non-tender goitre is noted. Blood tests reveal the following:

TSH	24.2 mU/l
Free T4	5.4 pmol/l

What is the most likely diagnosis?

- ☐ A. Primary atrophic hypothyroidism
- ☐ B. Pituitary failure
- ☐ C. De Quervain's thyroiditis
- ☐ D. Iodine deficiency
- ☐ E. Hashimoto's thyroiditis

Next question

Hashimoto's thyroiditis = hypothyroidism + goitre + anti-TPO

The combination of a goitre with hypothyroidism points to a diagnosis of Hashimoto's. De Quervain's thyroiditis typically causes a painful goitre.

**Hashimoto's thyroiditis**

Hashimoto's thyroiditis is an autoimmune disorder of the thyroid gland. It is typically associated with hypothyroidism although there may be a transient thyrotoxicosis in the acute phase. It is 10 times more common in women

**Features**

- features of hypothyroidism
- goitre: firm, non-tender
- anti-thyroid peroxidase and also anti-Tg antibodies

**Question 23 of 153**

Next

A 71-year-old woman with a history of type 2 diabetes mellitus presents with lethargy and polyuria. A diagnosis of hyperosmolar hyperglycaemic state is considered. Which one of the following findings would be least consistent with this diagnosis?

<input type="radio"/>	A. pH of 7.38
<input type="radio"/>	B. Ketones 1+ in urine
<input type="radio"/>	C. Serum osmolality of 310 mosmol/kg
<input type="radio"/>	D. Serum bicarbonate of 19 mmol/l
<input type="radio"/>	E. Glucose of 45 mmol/l

Next question

A trace of ketones may be found in hyperosmolar hyperglycaemic state. Serum osmolality is typically > 320 mosmol/kg

**Hyperosmolar hyperglycaemic state**

The American Diabetes Association criteria for the diagnosis of hyperosmolar hyperglycaemic state (HHS) is as follows:

- glucose > 33.3 mmol/l
- pH > 7.30
- serum bicarbonate > 15 mmol/l
- serum osmolality > 320 mosmol/kg
- traces of ketones may be present in urine

In patients with suspected insulinoma, which one of the following is considered the best investigation?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Oral glucose tolerance test    |
| <input type="radio"/> | B. Insulin tolerance test         |
| <input type="radio"/> | C. Early morning C-peptide levels |
| <input type="radio"/> | D. Glucagon stimulation test      |
| <input type="radio"/> | E. Supervised fasting             |

Next question

Insulinoma is diagnosed with supervised prolonged fasting

CT of the pancreas is also useful in demonstrating a lesion

## Insulinoma

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

### Basics

- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

### Features

- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

### Diagnosis

- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

### Management

- surgery
- diazoxide and somatostatin if patients are not candidates for surgery

**Question 25 of 153**

Next

A 54-year-old woman presents to the Emergency Department with confusion and fever. She has a past history of thyrotoxicosis previously treated with radioiodine therapy. On examination she has a pulse of 120/min regular, blood pressure 150/90 mmHg, temperature of 39.1°C and a respiratory rate of 18/min. Examination of the cardiorespiratory system is unremarkable and urine dipstick is clear. Blood results showed the following:

Free T4	84 pmol/l (normal range 10-22 pmol/l)
Free T3	29 pmol/l (2.5-5.5 pmol/l)
TSH	< 0.01 mU/l (0.5-4.0 mU/l)

Which one of the following does not have a role in the subsequent management?

- ☐ A. Lugol's iodine
- ☐ B. Propranolol
- ☐ C. Propylthiouracil
- ☐ D. Bicarbonate
- ☐ E. Dexamethasone

Next question

There is no indication for giving bicarbonate in this scenario.

**Thyroid storm**

Thyroid storm is a rare but life-threatening complication of thyrotoxicosis. It is typically seen in patients with established thyrotoxicosis and is rarely seen as the presenting feature. Iatrogenic thyroxine excess does not usually result in thyroid storm

Clinical features include:

- fever > 38.5°C
- tachycardia
- confusion and agitation
- nausea and vomiting
- hypertension
- heart failure
- abnormal liver function test

**Management**

- symptomatic treatment e.g. paracetamol
- treatment of underlying precipitating event
- anti-thyroid drugs: e.g. methimazole or propylthiouracil

- Lugol's iodine
- dexamethasone - e.g. 4mg IV qds - blocks the conversion of T4 to T3
- propranolol

A diabetic man is diagnosed as having painful diabetic neuropathy in his feet. He has no other medical history of note. What is the most suitable first-line treatment to relieve his pain?

<input type="radio"/>	A. Duloxetine
<input type="radio"/>	B. Gabapentin
<input type="radio"/>	C. Carbamazepine
<input type="radio"/>	D. Referral to pain management clinic
<input type="radio"/>	E. Pregabalin

[Next question](#)

### Diabetic neuropathy

NICE updated its guidance on the management of diabetic neuropathy in 2010:

- first-line: oral duloxetine. Oral amitriptyline if duloxetine is contraindicated.
- second-line treatment: if first-line treatment was with duloxetine, switch to amitriptyline or pregabalin, or combine with pregabalin. If first-line treatment was with amitriptyline, switch to or combine with pregabalin
- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

### Gastroparesis

- symptoms include erratic blood glucose control, bloating and vomiting
- management options include metoclopramide, domperidone or erythromycin (prokinetic agents)



A 46-year-old man presents as he is concerned about reduced libido, erectile dysfunction and excessive thirst. His wife also reports that he has 'no energy' and is generally listless. During the review of systems he also complains of pains in both hands. Which one of the following investigations is most likely to reveal the diagnosis?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Ferritin      |
| <input type="radio"/> | B. Testosterone  |
| <input type="radio"/> | C. Cortisol      |
| <input type="radio"/> | D. Blood glucose |
| <input type="radio"/> | E. Prolactin     |

Next question

The above patient has symptoms consistent with haemochromatosis. The excessive thirst is secondary to untreated diabetes mellitus. Diabetes mellitus itself would not normally cause reduced libido or arthralgia.

### Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6\*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

#### Epidemiology

- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

#### Presenting features

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	Irreversible complications
<ul style="list-style-type: none"> <li>• Cardiomyopathy</li> </ul>	<ul style="list-style-type: none"> <li>• Liver cirrhosis**</li> </ul>

- Skin pigmentation

- Diabetes mellitus
- Hypogonadotrophic hypogonadism
- Arthropathy

\*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

\*\*whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

A 64-year-old man with a history of type 2 diabetes mellitus is admitted with chest pain to the Emergency Department. An ECG shows ST elevation in the anterior leads and he is thrombolysed and transferred to the Coronary Care Unit (CCU). His usual medication includes simvastatin, gliclazide and metformin. How should his diabetes be managed whilst in CCU?

- |                                  |  |
|----------------------------------|--|
| <input type="radio"/>            | A. Stop metformin + continue gliclazide at a higher dose |
| <input type="radio"/>            | B. Subcutaneous insulin: basal-bolus regime              |
| <input type="radio"/>            | C. Continue metformin + gliclazide at same dose          |
| <input checked="" type="radio"/> | D. Intravenous insulin + stop metformin                  |
| <input type="radio"/>            | E. Subcutaneous insulin: biphasic insulin regime         |

Next question

The benefits of tight glycaemic control following a myocardial infarction were initially established by the DIGAMI study. These findings were not repeated in the later DIGAMI 2 study. However modern clinical practice is still that type 2 diabetics are converted to intravenous insulin in the immediate period following a myocardial infarction.

### Myocardial infarction: management

A number of studies over the past 10 years have provided an evidence for the management of ST-elevation myocardial infarction (STEMI)

In the absence of contraindications, all patients should be given

- aspirin
- clopidogrel: the two major studies (CLARITY and COMMIT) both confirmed benefit but used different loading doses (300mg and 75mg respectively)
- low molecular weight heparin

NICE suggest the following in terms of oxygen therapy:

- do not routinely administer oxygen, but monitor oxygen saturation using pulse oximetry as soon as possible, ideally before hospital admission. Only offer supplemental oxygen to:
- people with oxygen saturation (SpO<sub>2</sub>) of less than 94% who are not at risk of hypercapnic respiratory failure, aiming for SpO<sub>2</sub> of 94-98%
- people with chronic obstructive pulmonary disease who are at risk of hypercapnic respiratory failure, to achieve a target SpO<sub>2</sub> of 88-92% until blood gas analysis is available.

Primary percutaneous coronary intervention (PCI) has emerged as the gold-standard treatment for STEMI but is not available in all centres. Thrombolysis should be performed in patients without access to primary PCI

With regards to thrombolysis:

- tissue plasminogen activator (tPA) has been shown to offer clear mortality benefits over streptokinase
- tenecteplase is easier to administer and has been shown to have non-inferior efficacy to alteplase with a similar adverse effect profile

An ECG should be performed 90 minutes following thrombolysis to assess whether there has been a greater than 50% resolution in the ST elevation

- if there has not been adequate resolution then rescue PCI is superior to repeat thrombolysis
- for patients successfully treated with thrombolysis PCI has been shown to be beneficial. The optimal timing of this is still under investigation

**Question 29 of 153**

Next

An 18-year-old girl is admitted to the Emergency Department with an episode of sweating and dizziness. She is brought in by her father who has type 2 diabetes mellitus as he is worried she may be diabetic. He describes a number of similar episodes for the past two weeks. Her BM on admission is 1.9 mmol/l so the following bloods are taken:

Plasma glucose	1.8 mmol/l
Insulin	15 mg/ml (6-10 mg/ml)
Proinsulin	22% (22-24%)
C-peptide	0.15 nmol/l (0.2-0.4 nmol/l)

What is the most likely diagnosis?

- ☐ A. Diabetes mellitus
- ☐ B. Insulinoma
- ☐ C. Nesidioblastosis
- ☒ D. Insulin abuse
- ☐ E. Sulfonylurea abuse

Next question

The raised insulin with low c-peptide level points to a diagnosis of insulin abuse. C-peptide levels would be raised in a patient following sulfonylurea abuse

**Hypoglycaemia****Causes**

- insulinoma - increased ratio of proinsulin to insulin
- self-administration of insulin/sulphonylureas
- liver failure
- Addison's disease
- alcohol

**Other possible causes in children**

- nesidioblastosis - beta cell hyperplasia

A 58-year-old man comes for review in the diabetes clinic. He was diagnosed as having type 2 diabetes mellitus around 10 years ago and currently only takes gliclazide and simvastatin. A recent trial of metformin was unsuccessful due to gastrointestinal side-effects. He works as an accountant, is a non-smoker and his BMI is 39 kg/m<sup>2</sup>. His annual bloods show the following:

Na <sup>+</sup>	138 mmol/l
K <sup>+</sup>	4.1 mmol/l
Urea	4.3 mmol/l
Creatinine	104 µmol/l
HbA1c	7.8%

What is the most appropriate next step in management?

- ☐ A. Add pioglitazone
- ☐ B. Add exenatide
- ☐ C. Add acarbose
- ☐ D. Add repaglinide
- ☐ E. Switch gliclazide for sitagliptin

Next question

Pioglitazone is a possible option but may contribute to his obesity. There are also increasing concerns regarding the safety profile of thiazolidinediones, although the majority of negative data relates to rosiglitazone. Exenatide generally causes weight loss and is therefore useful in obese diabetics with suboptimal glycaemic control

### Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

#### Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

- the general target for patients is 48 mmol/mol (DCCT = 6.5%). HbA1c levels below 48 mmol/mol (DCCT = 6.5%) should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

#### Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first\*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 48 mmol/mol (DCCT = 6.5%)
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 58 mmol/mol (DCCT = 7.5%) then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% at 6 months)

#### Starting insulin

- usually commenced if HbA1c > 58 mmol/mol (DCCT = 7.5%)
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

#### Other risk factor modification

- current NICE guidelines suggest giving aspirin to all patients > 50 years and to younger patients with other significant risk factors. However, recent evidence does not support this approach. The 2010 SIGN guidelines do not advocate the use of aspirin for primary prevention in diabetics
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reached consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

\*many local protocols now recommend starting metformin upon diagnosis

What is the mechanism of action of thiazolidinediones?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. PPAR-gamma receptor antagonist         |
| <input type="radio"/> | B. PPAR-alpha receptor antagonist         |
| <input type="radio"/> | C. PPAR-alpha receptor agonist            |
| <input type="radio"/> | D. PPAR-gamma receptor agonist            |
| <input type="radio"/> | E. Increases endogenous insulin secretion |

Next question

Glitazones are agonists of PPAR-gamma receptors, reducing peripheral insulin resistance

### Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance. Rosiglitazone was withdrawn in 2010 following concerns about the cardiovascular side-effect profile.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

#### Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- bladder cancer: recent studies have showed an increased risk of bladder cancer in patients taking pioglitazone (hazard ratio 2.64)

#### NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months



A 27-year-old female develops eye pain and reduced visual acuity following the initiation of treatment for her recently diagnosed Grave's disease. Which one of the following treatments is likely to have been started?

<input type="radio"/>	A. Radioiodine treatment
<input type="radio"/>	B. Thyroidectomy
<input type="radio"/>	C. Propylthiouracil
<input type="radio"/>	D. Carbimazole and thyroxine
<input type="radio"/>	E. Carbimazole

[Next question](#)

Radioiodine treatment may lead to the development / worsening of thyroid eye disease in up to 15% of patients with Grave's disease

### Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

#### Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

#### Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

#### Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

An obese 48-year-old man presents with lethargy and polydipsia. What is the minimum HbA1c that would be diagnostic of type 2 diabetes mellitus?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Cannot use HbA1c for diagnosis |
| <input type="radio"/> | B. 6.0% (42 mmol/mol)             |
| <input type="radio"/> | C. 6.3% (45 mmol/mol)             |
| <input type="radio"/> | D. 6.5% (48 mmol/mol)             |
| <input type="radio"/> | E. 7.0% (53 mmol/mol)             |

[Next question](#)

Diabetes mellitus - HbA1c of 6.5% or greater is now diagnostic (WHO 2011)

### Diabetes mellitus: diagnosis

The following is based on the World Health Organisation (WHO) 2006 guidelines.

#### Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

In 2011 WHO released supplementary guidance on the use of HbA1c on the diagnosis of diabetes:

- a HbA1c of greater than or equal to 6.5% (48 mmol/mol) is diagnostic of diabetes mellitus
- a HbA1c value of less than 6.5% does not exclude diabetes (i.e. it is not as sensitive as fasting samples for detecting diabetes)
- in patients without symptoms, the test must be repeated to confirm the diagnosis
- it should be remembered that misleading HbA1c results can be caused by increased red cell turnover (for example anaemia, haemoglobinopathies and pregnancy)

#### Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

A 28-year-old woman with polycystic ovarian syndrome consults you as she is having problems becoming pregnant. She has a past history of oligomenorrhea and has previously recently stopped taking a combined oral contraceptive pill. Despite stopping the pill 6 months ago she is still not having regular periods. Her body mass index is 28 kg/m<sup>2</sup>. Apart from advising her to lose weight, which one of the following interventions is most effective in increasing her chances of conceiving?

<input type="radio"/>	A. Metformin
<input type="radio"/>	B. Bromocriptine
<input type="radio"/>	C. Laparoscopic ovarian cauterization
<input checked="" type="radio"/>	D. Clomifene
<input type="radio"/>	E. Orlistat

Next question

Infertility in PCOS - clomifene is superior to metformin

Whilst metformin has a role in the management of infertility it should be used second-line to anti-oestrogens such as clomifene. Similar questions to this often appear in which clomifene is not an option, in this case metformin is clearly the right answer.

### Polycystic ovarian syndrome: management

Polycystic ovarian syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. Management is complicated and problem based partly because the aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome.

#### General

- weight reduction if appropriate
- if a woman requires contraception then a combined oral contraceptive (COC) pill may help regulate her cycle and induce a monthly bleed (see below)

#### Hirsutism and acne

- a COC pill may be used help manage hirsutism. Possible options include a third generation COC which has fewer androgenic effects or co-cyprindiol which has an anti-androgen action. Both of these types of COC may carry an increased risk of venous thromboembolism
- if doesn't respond to COC then topical eflornithine may be tried
- spironolactone, flutamide and finasteride may be used under specialist supervision

## Infertility

- weight reduction if appropriate
- the management of infertility in patients with PCOS should be supervised by a specialist. There is an ongoing debate as to whether metformin, clomifene or a combination should be used to stimulate ovulation
- a 2007 trial published in the New England Journal of Medicine suggested clomifene was the most effective treatment. There is a potential risk of multiple pregnancies with anti-oestrogen\* therapies such as clomifene. The RCOG published an opinion paper in 2008 and concluded that on current evidence metformin is

not a first line treatment of choice in the management of PCOS

- metformin is also used, either combined with clomifene or alone, particularly in patients who are obese
- gonadotrophins

\*work by occupying hypothalamic oestrogen receptors without activating them. This interferes with the binding of oestradiol and thus prevents negative feedback inhibition of FSH secretion

**Question 35 of 153**

Next

A 55-year-old woman is investigated following an osteoporotic hip fracture. The following results are obtained:

TSH	< 0.05 mu/l
Free T4	29 pmol/l

Which one of the following autoantibodies is most likely to be present?

- ☐ A. Anti-TSH receptor stimulating autoantibodies
- ☐ B. Anti-nuclear antibodies
- ☐ C. Anti-thyroglobulin autoantibodies
- ☐ D. Anti-microsomal antibodies
- ☐ E. Anti-thyroid peroxidase autoantibodies

Next question

Anti-TSH receptor stimulating autoantibodies (often referred to as Thyroid Stimulating Immunoglobulins) are almost diagnostic of Graves' disease, the most common cause of thyrotoxicosis in the UK

**Graves' disease: features**

Graves' disease is the most common cause of thyrotoxicosis. It is typically seen in women aged 30-50 years.

**Features**

- typical features of thyrotoxicosis
- specific signs limited to Grave's (see below)

**Features seen in Graves' but not in other causes of thyrotoxicosis**

- eye signs (30% of patients): exophthalmos, ophthalmoplegia
- pretibial myxoedema
- thyroid acropachy

**Autoantibodies**

- anti-TSH receptor stimulating antibodies (90%)
- anti-thyroid peroxidase antibodies (50%)

**Question 36 of 153**

Next

A 45-year-old man presents with bitemporal hemianopia and spade-like hands. What is the definite test to confirm the diagnosis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Early morning growth hormone                                 |
| <input type="radio"/> | B. Insulin tolerance test                                       |
| <input type="radio"/> | C. Oral glucose tolerance test with growth hormone measurements |
| <input type="radio"/> | D. Random insulin-like growth factor 1 (IGF-1)                  |
| <input type="radio"/> | E. Short ACTH test  |

Next question

The diagnostic test for acromegaly is an oral glucose tolerance with growth hormone measurements

**Acromegaly: investigations**

Growth hormone (GH) levels vary during the day and are therefore not diagnostic. The definitive test is the oral glucose tolerance (OGTT) with serial GH measurements. Serum IGF-1 may also be used as a screening test and is sometimes used to monitor disease

Oral glucose tolerance test

- in normal patients GH is suppressed to  $< 2 \text{ mu/L}$  with hyperglycaemia
- in acromegaly there is no suppression of GH
- may also demonstrate impaired glucose tolerance which is associated with acromegaly

A pituitary MRI may demonstrate a pituitary tumour

A 25-year-old Asian woman who is 26 weeks pregnant has an oral glucose tolerance test (OGTT). This was requested due to a combination of her ethnicity and a background of obesity. A recent ultrasound shows that the fetus is large for dates. The following results are obtained:

Time (hours)	Blood glucose (mmol/l)
0	9.2
2	14.2

What is the most appropriate management?

- ☐ A. Start insulin
- ☐ B. Give advice about a diabetic diet
- ☐ C. Give advice about a diabetic diet + repeat OGTT in 4 weeks
- ☐ D. Start gliclazide
- ☐ E. Start insulin + aspirin

Next question

Insulin should be started straight away given the blood glucose levels and evidence of macrosomia. Some endocrinologists would consider using either metformin or glibenclamide but gliclazide (option D) is not mentioned in the NICE guidelines.

### Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies

Risk factors for gestational diabetes

- BMI of  $> 30 \text{ kg/m}^2$
- previous macrosomic baby weighing 4.5 kg or above.
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes

- if a woman has had gestational diabetes previously an oral glucose tolerance test (OGTT) should be performed at 16-18 weeks and at 28 weeks if the first test is normal
- women with any of the other risk factors should be offered an OGTT at 24-28 weeks



- currently the same WHO diagnostic criteria are used as for non-pregnant patients. There is however increasing evidence that a lower threshold should be used as treating borderline patients improves both maternal and neonatal outcomes

NICE issued guidelines on the management of diabetes mellitus in pregnancy in 2008

#### Management of pre-existing diabetes

- weight loss for women with BMI of  $> 27 \text{ kg/m}^2$
- stop oral hypoglycaemic agents, apart from metformin, and commence insulin
- folic acid 5 mg/day from pre-conception to 12 weeks gestation
- detailed anomaly scan at 18-20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy

#### Management of gestational diabetes

- responds to changes in diet and exercise in around 80% of women
- oral hypoglycaemic agents (metformin or glibenclamide) or insulin injections are needed if blood glucose control is poor or there is any evidence of complications (e.g. macrosomia)
- there is increasing evidence that oral hypoglycaemic agents are both safe and give similar outcomes to insulin
- hypoglycaemic medication should be stopped following delivery
- a fasting glucose should be checked at the 6 week postnatal check

**Question 38 of 153**

Next

A 33-year-old woman is referred to the endocrinology clinic with thyrotoxicosis. Recent blood tests show the following:

TSH	< 0.05 mu/l
Free T4	25 pmol/l
Anti-thyroid peroxidase antibodies	115 IU/mL (< 35 IU/mL)

A smooth, non-tender goitre is noted on examination the neck. The patient also has exophthalmos although there is no ophthalmoplegia, no reduction in visual acuity and no eye symptoms present.

What is the most appropriate management?

- ☐ A. Radioiodine treatment
- ☐ B. Carbimazole
- ☐ C. Propranolol
- ☐ D. Fine needle aspiration biopsy of the thyroid gland
- ☐ E. Intravenous corticosteroids

Next question

This patient has Graves' disease as evidenced by the thyrotoxicosis, goitre, thyroid eye disease and anti-thyroid peroxidase antibodies.

Radioiodine treatment should be avoided given the presence of thyroid eye disease so carbimazole is a better treatment option.

If her eye disease was severe then an ophthalmologist should be consulted. Options for severe thyroid eye disease include systemic steroids and radiotherapy.

**Graves' disease: management**

Despite many trials there is no clear guidance on the optimal management of Graves' disease. Treatment options include titration of anti-thyroid drugs (ATDs, for example carbimazole), block-and-replace regimes, radioiodine treatment and surgery. Propranolol is often given initially to block adrenergic effects

**ATD titration**

- carbimazole is started at 40mg and reduced gradually to maintain euthyroidism
- typically continued for 12-18 months
- patients following an ATD titration regime have been shown to suffer fewer side-effects than those on a block-and-replace regime

## Block-and-replace

- carbimazole is started at 40mg
- thyroxine is added when the patient is euthyroid
- treatment typically lasts for 6-9 months

The major complication of carbimazole therapy is agranulocytosis

## Radioiodine treatment

- contraindications include pregnancy (should be avoided for 4-6 months following treatment) and age < 16 years. Thyroid eye disease is a relative contraindication, as it may worsen the condition
- the proportion of patients who become hypothyroid depends on the dose given, but as a rule the majority of patient will require thyroxine supplementation after 5 years

**Question 39 of 153**

Next

A 45-year-old man is reviewed in the diabetes clinic. The following results are obtained:

Urinalysis	NAD
HbA1c	8.6%

Gliclazide is added to the metformin he already takes. What is the minimum time period after which the HbA1c should be repeated ?

- ☐ A. 6 months
- ☐ B. 1 month
- ☐ C. 2 weeks
- ☐ D. 3 months
- ☐ E. 4 months

Next question

HbA1C - recheck after 2-3 months

A more accurate answer would probably be 2 months but this is not given as an option. See the explanation below

**Glycosylated haemoglobin**

Glycosylated haemoglobin (HbA1c) is the most widely used measure of long-term glycaemic control in diabetes mellitus. HbA1c is produced by the glycosylation of haemoglobin at a rate proportional to the glucose concentration. The level of HbA1c therefore is dependant on

- red blood cell lifespan
- average blood glucose concentration

HbA1c is generally thought to reflect the blood glucose over the previous '2-3 months' although there is some evidence it is weighed more strongly to glucose levels of the past 2-4 weeks

The relationship between HbA1c and average blood glucose is complex but has been studied by the Diabetes Control and Complications Trial (DCCT). A new internationally standardised method for reporting HbA1c has been developed by the International Federation of Clinical Chemistry (IFCC). This will report HbA1c in mmol per mol of haemoglobin without glucose attached.

HbA1c (%)	Average plasma glucose (mmol/l)	IFCC-HbA1c (mmol/mol)
5	5.5	
6	7.5	42
7	9.5	53
8	11.5	64
9	13.5	75
10	15.5	
11	17.5	
12	19.5	

From the above we can see that average plasma glucose =  $(2 * \text{HbA1c}) - 4.5$

Which one of the following is not associated with primary hyperparathyroidism?

<input type="radio"/>	A. Hypotension
<input type="radio"/>	B. Multiple endocrine neoplasia type 1
<input type="radio"/>	C. Multiple endocrine neoplasia type 2a
<input type="radio"/>	D. Depression
<input type="radio"/>	E. Pancreatitis

Next question

Primary hyperparathyroidism is associated with hypertension

### Primary hyperparathyroidism

In exams primary hyperparathyroidism is stereotypically seen in elderly females with an unquenchable thirst and an inappropriately normal or raised parathyroid hormone level. It is most commonly due to a solitary adenoma

Causes of primary hyperparathyroidism

- 80%: solitary adenoma
- 15%: hyperplasia
- 4%: multiple adenoma
- 1%: carcinoma

Features - 'bones, stones, abdominal groans and psychic moans'

- polydipsia, polyuria
- peptic ulceration/constipation/pancreatitis
- bone pain/fracture
- renal stones
- depression
- hypertension

Associations

- hypertension
- multiple endocrine neoplasia: MEN I and II

Investigations

- raised calcium, low phosphate

- PTH may be raised or normal
- technetium-MIBI subtraction scan

## Treatment

- total parathyroidectomy

A 36-year-old female with a BMI of 34 kg/m<sup>2</sup> is reviewed after managing to lose 3 kg in the past month. She asks about the possibility of starting a drug to help her lose weight. What is the primary mode of action of orlistat?

<input type="radio"/>	A. Leptin antagonist
<input type="radio"/>	B. Pancreatic lipase inhibitor
<input type="radio"/>	C. Blocks intestinal absorption of lipids
<input type="radio"/>	D. HMG-CoA reductase inhibitor
<input type="radio"/>	E. Centrally-acting appetite suppressant

Next question

The primary mode of action of orlistat is to inhibit pancreatic lipases, which in turn will decrease the absorption of lipids from the intestine

### Obesity: therapeutic options

The management of obesity consists of a step-wise approach:

- conservative: diet, exercise
- medical
- surgical

Orlistat is a pancreatic lipase inhibitor used in the management of obesity. Adverse effects include faecal urgency/incontinence and flatulence. A lower dose version is now available without prescription ('Alli'). NICE have defined criteria for the use of orlistat. It should only be prescribed as part of an overall plan for managing obesity in adults who have:

- BMI of 28 kg/m<sup>2</sup> or more with associated risk factors, or
- BMI of 30 kg/m<sup>2</sup> or more
- continued weight loss e.g. 5% at 3 months
- orlistat is normally used for < 1 year

### Sibutramine

- withdrawn January 2010 by the European Medicines Agency due to an increased risk of cardiovascular events
- centrally acting appetite suppressant (inhibits uptake of serotonin and noradrenaline at hypothalamic sites that regulate food intake)
- adverse effects include hypertension (monitor blood pressure and pulse during treatment), constipation, headache, dry mouth, insomnia and anorexia
- contraindicated in psychiatric illness, hypertension, IHD, stroke, arrhythmias

Rimonabant, a specific CB1 cannabinoid receptor antagonist, was withdrawn in October 2008 after the European Medicines Agency warned of serious psychiatric problems including suicide



Which of the following secondary causes of hyperlipidaemia result in predominantly hypercholesterolaemia, as opposed to hypertriglyceridaemia?

<input type="radio"/>	A. Diabetes mellitus
<input type="radio"/>	B. Bendrofluazide
<input type="radio"/>	C. Nephrotic syndrome
<input type="radio"/>	D. Alcohol
<input type="radio"/>	E. Obesity

[Next question](#)

Hypercholesterolaemia rather than hypertriglyceridaemia: nephrotic syndrome, cholestasis, hypothyroidism

### Hyperlipidaemia: secondary causes

Causes of predominantly hypertriglyceridaemia

- diabetes mellitus (types 1 and 2)
- obesity
- alcohol
- chronic renal failure
- drugs: thiazides, non-selective beta-blockers, unopposed oestrogen
- liver disease

Causes of predominantly hypercholesterolaemia

- nephrotic syndrome
- cholestasis
- hypothyroidism

Which one of the following is not part of the diagnostic criteria for the metabolic syndrome?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. High triglycerides |
| <input type="radio"/> | B. Low HDL            |
| <input type="radio"/> | C. High LDL           |
| <input type="radio"/> | D. Central obesity    |
| <input type="radio"/> | E. Hypertension       |

Next question

High LDL levels are not part of the World Health Organization or International Diabetes Federation diagnostic criteria

### Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europic men and > 80cm for Europic women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure:  $> 140/90$  mmHg
- dyslipidaemia: triglycerides:  $> 1.695$  mmol/L and/or high-density lipoprotein cholesterol (HDL-C)  $< 0.9$  mmol/L (male),  $< 1.0$  mmol/L (female)
- central obesity: waist:hip ratio  $> 0.90$  (male),  $> 0.85$  (female), and/or body mass index  $> 30$  kg/m<sup>2</sup>
- microalbuminuria: urinary albumin excretion ratio  $> 20$  mg/min or albumin:creatinine ratio  $> 30$  mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

**Question 44 of 153**

Next

A 45-year-old female is reviewed in the medical clinic with a two month history of lethargy. Blood tests reveal the following:

Na <sup>+</sup>	129 mmol/l
K <sup>+</sup>	5.1 mmol/l
Urea	5.3 mmol/l
Creatinine	99 µmol/l
Total T4	66 nmol/l

Which one of the following investigations is most likely to reveal the diagnosis?

- ☐ A. Serum glucose
- ☐ B. TSH
- ☐ C. Free T4
- ☐ D. Overnight dexamethasone suppression test
- ☐ E. Short synacthen test

Next question

The short synacthen test is the best test to diagnose Addison's disease

Hyponatraemia and a high potassium in a patient with lethargy is highly suggestive of Addison's disease. The thyroxine level is slightly low and she may indeed have co-existing hypothyroidism but this would not explain the high potassium

Many labs have an upper reference range for potassium of 5.5 mmol/l, but in the context of the other results hypoadrenalism should be suspected

**Addison's disease: investigations**

In a patient with suspected Addison's disease the definite investigation is a ACTH stimulation test (short Synacthen test). Plasma cortisol is measured before and 30 minutes after giving Synacthen 250ug IM. Adrenal autoantibodies such as anti-21-hydroxylase may also be demonstrated

Associated electrolyte abnormalities

- hyperkalaemia
- hyponatraemia
- hypoglycaemia
- metabolic acidosis

Which one of the following is not an indication for treating a patient with subclinical hypothyroidism?

<input type="radio"/>	A. Previous treatment of Graves' disease
<input type="radio"/>	B. TSH > 10
<input type="radio"/>	C. Raised ESR
<input type="radio"/>	D. Positive thyroid autoantibodies
<input type="radio"/>	E. Other autoimmune disorder

Next question

## Subclinical hypothyroidism

### Basics

- TSH raised but T3, T4 normal
- no obvious symptoms

### Significance

- risk of progressing to overt hypothyroidism is 2-5% per year (higher in men)
- risk increased by presence of thyroid autoantibodies

### Treat if

- TSH > 10
- thyroid autoantibodies positive
- other autoimmune disorder
- previous treatment of Graves' disease

**Question 46 of 153**

Next

A 56-year-old lady with a BMI of 27 is reviewed in the diabetic clinic due to poor glycaemic control. She is currently being treated with gliclazide 160mg bd. Her latest bloods show:

Na <sup>+</sup>	139 mmol/l
K <sup>+</sup>	4.1 mmol/l
Urea	8.4 mmol/l
Creatinine	170 µmol/l
ALT	25 iu/l
γGT	33 iu/l
HbA1c	9.4%

Which one of the following medications should be added next?

<input type="radio"/>	A. Guar gum
<input type="radio"/>	B. Pioglitazone
<input type="radio"/>	C. Metformin
<input type="radio"/>	D. Acarbose
<input type="radio"/>	E. Repaglinide

Next question

Given that she is overweight metformin would be a natural choice to add. The creatinine however is elevated so pioglitazone is the next best option

One possible drawback of using pioglitazone is that it may lead to weight gain, especially given her BMI is already 27

**Thiazolidinediones**

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance. Rosiglitazone was withdrawn in 2010 following concerns about the cardiovascular side-effect profile.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

**Adverse effects**

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin

- recent studies have indicated an increased risk of fractures
- bladder cancer: recent studies have showed an increased risk of bladder cancer in patients taking pioglitazone (hazard ratio 2.64)

#### NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

**Question 47 of 153**

Next

A 30-year-old female is diagnosed with having Grave's disease. What is her chance of developing thyroid eye disease?

<input type="radio"/>	A. 2-5%
<input type="radio"/>	B. 5-10%
<input type="radio"/>	C. 10-15%
<input type="radio"/>	D. 15-25%
<input type="radio"/>	E. 25-50%

Next question

**Thyroid eye disease**

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turn causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

**Prevention**

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

**Features**

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

**Management**

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery



A 43-year-old man requests a 'medical' as he is concerned about his risk of heart disease. His father died at the age of 45-years following a myocardial infarction. His lipid profile is as follows:

HDL	1.4 mmol/l
LDL	5.7 mmol/l
Triglycerides	2.3 mmol/l
Total cholesterol	8.2 mmol/l

Clinical examination reveals tendon xanthomata around his ankles. What is the most likely diagnosis?

- ☐ A. Familial hypercholesterolaemia (heterozygous)
- ☐ B. Nephrotic syndrome
- ☐ C. Mixed hyperlipidaemia
- ☐ D. Familial hypercholesterolaemia (homozygous)
- ☐ E. Hypothyroidism

Next question

The presence of tendon xanthomata and cholesterol levels meet the diagnostic criteria for familial hypercholesterolaemia. Homozygous familial hypercholesterolaemia is exceedingly rare - most patients die in their teenage years from a myocardial infarction.

### Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that is thought to affect around 1 in 500 people. It results in high levels of LDL-cholesterol which, if untreated, may cause early cardiovascular disease (CVD). FH is caused by mutations in the gene which encodes the LDL-receptor protein.

Clinical diagnosis is now based on the **Simon Broome criteria**:

- in adults total cholesterol (TC) > 7.5 mmol/l and LDL-C > 4.9 mmol/l or children TC > 6.7 mmol/l and LDL-C > 4.0 mmol/l, plus:
- for definite FH: tendon xanthoma in patients or 1st or 2nd degree relatives or DNA-based evidence of FH
- for possible FH: family history of myocardial infarction below age 50 years in 2nd degree relative, below age 60 in 1st degree relative, or a family history of raised cholesterol levels

### Management

- the use of CVD risk estimation using standard tables is not appropriate in FH as they do not accurately reflect the risk of CVD
- referral to a specialist lipid clinic is usually required
- the maximum dose of potent statins are usually required

- first-degree relatives have a 50% chance of having the disorder and should therefore be offered screening. This includes children who should be screened by the age of 10 years if there is one affected parent
- statins should be discontinued in women 3 months before conception due to the risk of congenital defects

**Question 49 of 153**

Next

A 29-year-old female who is 14 weeks into her first pregnancy is investigated for excessive sweating and tremor. Blood tests reveal the following:

TSH	< 0.05 mu/l
T4	188 nmol/l

What is the most appropriate management?

- ☐ A. Immediate surgery
- ☐ B. Carbimazole
- ☐ C. Surgery at start of third trimester
- ☐ D. Propylthiouracil
- ☐ E. Radioiodine

Next question

Propylthiouracil is traditionally taught as the antithyroid drug of choice in pregnancy. This approach was supported by the 2007 Endocrine Society consensus guidelines. It also has the advantage of being excreted to a lesser extent than carbimazole in breast milk.

Despite this some endocrinologists use carbimazole and the BNF states both drugs may be used in pregnancy. Carbimazole has rarely been associated with aplasia cutis of the neonate

**Pregnancy: thyroid problems**

In pregnancy there is an increase in the levels of thyroxine-binding globulin (TBG). This causes an increase in the levels of total thyroxine but does not affect the free thyroxine level

**Thyrotoxicosis**

Untreated thyrotoxicosis increases the risk of fetal loss, maternal heart failure and premature labour

Graves' disease is the most common cause of thyrotoxicosis in pregnancy. It is also recognised that activation of the TSH receptor by HCG may also occur - often termed transient gestational hyperthyroidism. HCG levels will fall in second and third trimester

**Management**

- propylthiouracil has traditionally been the antithyroid drug of choice. This approach was supported by the 2007 Endocrine Society consensus guidelines
- maternal free thyroxine levels should be kept in the upper third of the normal reference range to avoid fetal hypothyroidism

- thyrotrophin receptor stimulating antibodies should be checked at 30-36 weeks gestation - helps to determine risk of neonatal thyroid problems
- block-and-replace regimes should not be used in pregnancy
- radioiodine therapy is contraindicated

## **Hypothyroidism**

### Key points

- thyroxine is safe during pregnancy
- serum thyroid stimulating hormone measured in each trimester and 6-8 weeks post-partum
- some women require an increased dose of thyroxine during pregnancy
- breast feeding is safe whilst on thyroxine

A 33-year-old female is referred to endocrinology with thyrotoxicosis. Following a discussion of management options she elects to have radioiodine therapy. Which one of the following is the most likely adverse effect?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Hypothyroidism                       |
| <input type="radio"/> | B. Thyroid malignancy                   |
| <input type="radio"/> | C. Agranulocytosis                      |
| <input type="radio"/> | D. Oesophagitis                         |
| <input type="radio"/> | E. Precipitation of thyroid eye disease |

Next question

It is well documented that radioiodine therapy can precipitate thyroid eye disease but a majority of patients will eventually require thyroxine replacement

### Graves' disease: management

Despite many trials there is no clear guidance on the optimal management of Graves' disease. Treatment options include titration of anti-thyroid drugs (ATDs, for example carbimazole), block-and-replace regimes, radioiodine treatment and surgery. Propranolol is often given initially to block adrenergic effects

#### ATD titration

- carbimazole is started at 40mg and reduced gradually to maintain euthyroidism
- typically continued for 12-18 months
- patients following an ATD titration regime have been shown to suffer fewer side-effects than those on a block-and-replace regime

#### Block-and-replace

- carbimazole is started at 40mg
- thyroxine is added when the patient is euthyroid
- treatment typically lasts for 6-9 months

The major complication of carbimazole therapy is agranulocytosis

#### Radioiodine treatment

- contraindications include pregnancy (should be avoided for 4-6 months following treatment) and age < 16 years. Thyroid eye disease is a relative contraindication, as it may worsen the condition
- the proportion of patients who become hypothyroid depends on the dose given, but as a rule the majority of patient will require thyroxine supplementation after 5 years

A 24-year-old female with a history of type 1 diabetes mellitus presents to the Emergency Department with vomiting and abdominal pain. Finger-prick testing estimates the blood sugar to be 25 mmol/l. Arterial blood gases record a pH of 7.22. On examination the patient is dehydrated and weighs 80 kg. An intravenous line is sited and bloods are sent. One litre of 0.9% saline is infused and an intravenous insulin pump is set-up. What rate should insulin be initially given?

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. 10 unit / hour |
| <input type="radio"/> | B. 1 unit / hour  |
| <input type="radio"/> | C. 2 unit / hour  |
| <input type="radio"/> | D. 6 unit / hour  |
| <input type="radio"/> | E. 8 unit / hour  |

[Next question](#)

The Joint British Diabetes Societies produced guidelines in 2010 recommending starting the insulin infusion at a rate of 0.1 unit/kg/hour.

### Diabetic ketoacidosis

The most common precipitating factors of diabetic ketoacidosis (DKA) are infection, missed insulin doses and myocardial infarction

American Diabetes Association diagnostic criteria are as follows:

- blood glucose >13.8 mmol/l
- pH < 7.30
- serum bicarbonate <18 mmol/l
- anion gap > 10
- ketonaemia

### Management

- fluid replacement: most patients with DKA are deplete around 5-8 litres. Isotonic saline is used initially
- insulin: an intravenous infusion should be started at 0.1 unit/kg/hour. Once blood glucose is < 15 mmol/l an infusion of 5% dextrose should be started
- correction of hypokalaemia

### Complications of DKA and its treatment

- gastric stasis
- cerebral oedema
- thromboembolism
- acute respiratory distress syndrome
- acute renal failure

**Question 52 of 153**

Next

A 60-year-old man who is known to have lung cancer comes for review. For the past three weeks he has lost his appetite, has been feeling sick and generally feels tired. On examination he appears to be mildly dehydrated.

You order some blood tests:

Calcium	3.12 mmol/l
Albumin	40 g/l
Glucose (random)	6.7 mmol/l
Urea	10.2 mmol/l
Creatinine	115 µmol/l

Which one of his existing medications is most likely to be contributing to his presentation?

<input type="radio"/>	A. Amlodipine
<input type="radio"/>	B. Simvastatin
<input type="radio"/>	C. Bendroflumethiazide
<input type="radio"/>	D. Aspirin
<input type="radio"/>	E. Lisinopril

Next question

Thiazides cause hypercalcaemia

**Hypercalcaemia: causes**

The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

- sarcoidosis\*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, calcium containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone\*\*

\*other causes of granulomas may lead to hypercalcaemia e.g. Tuberculosis and histoplasmosis

\*\*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

A 42-year-old man presents to his GP feeling generally unwell. For the past three months he has been experiencing daily frontal headaches which have not been helped by regular paracetamol. He has also noticed some unusual symptoms such as his wedding ring no longer fitting, his shoe size apparently increasing and a small amount of milky discharge from both nipples. On examination his blood pressure is 168/96 mmHg. What is the most likely diagnosis?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Pheochromocytoma   |
| <input type="radio"/> | B. Cushing's syndrome |
| <input type="radio"/> | C. Diabetes insipidus |
| <input type="radio"/> | D. Macroprolactinoma  |
| <input type="radio"/> | E. Acromegaly         |

[Next question](#)

### Acromegaly: features

In acromegaly there is excess growth hormone secondary to a pituitary adenoma in over 95% of cases. A minority of cases are caused by ectopic GHRH or GH production by tumours e.g. pancreatic

#### Features

- coarse facial appearance, spade-like hands, increase in shoe size
- large tongue, prognathism, interdental spaces
- excessive sweating and oily skin
- features of pituitary tumour: hypopituitarism, headaches, bitemporal hemianopia
- raised prolactin in 1/3 of cases --> galactorrhoea
- 6% of patients have MEN-1

#### Complications

- hypertension
- diabetes (>10%)
- cardiomyopathy
- colorectal cancer



Which one of the following statements regarding the metabolic syndrome is correct?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. The WHO criteria are used to define impaired glucose tolerance  |
| <input type="radio"/> | B. The central pathophysiological change is thought to be reduced insulin production   |
| <input type="radio"/> | C. A diagnosis cannot be made without weighing the patient   |
| <input type="radio"/> | D. A raised LDL concentration is one of the key criteria in most definitions   |
| <input type="radio"/> | E. Decisions on cardiovascular risk factor modification should be made regardless of whether patients meet the criteria for metabolic syndrome |

Next question

Decisions on primary prevention of cardiovascular disease should be made using standard tools and are not dependant on whether a diagnosis of metabolic syndrome is made.

### Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure:  $> 140/90$  mmHg
- dyslipidaemia: triglycerides:  $> 1.695$  mmol/L and/or high-density lipoprotein cholesterol (HDL-C)  $< 0.9$  mmol/L (male),  $< 1.0$  mmol/L (female)
- central obesity: waist:hip ratio  $> 0.90$  (male),  $> 0.85$  (female), and/or body mass index  $> 30$  kg/m<sup>2</sup>
- microalbuminuria: urinary albumin excretion ratio  $> 20$  mg/min or albumin:creatinine ratio  $> 30$  mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

A 43-year-old man is found to have a phaeochromocytoma. Which anti-hypertensive medication should be started first?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Propranolol      |
| <input type="radio"/> | B. Ramipril         |
| <input type="radio"/> | C. Atenolol         |
| <input type="radio"/> | D. Phenoxybenzamine |
| <input type="radio"/> | E. Doxazosin        |

[Next question](#)

**PH**aeochromocytoma - give **PH**enoxybenzamine before beta-blockers

Phenoxybenzamine is a non-selective alpha-adrenoceptor antagonist and should be started before a beta-blocker is introduced

There is ongoing debate about the optimal medical management of phaeochromocytoma, with the suggestion that antihypertensive treatment regimes other than non specific alpha-blockade are just as effective and safe. There are however no trials to provide an answer to this question yet

### Phaeochromocytoma

Phaeochromocytoma is a rare catecholamine secreting tumour. About 10% are familial and may be associated with MEN type II, neurofibromatosis and von Hippel-Lindau syndrome

#### Basics

- bilateral in 10%
- malignant in 10%
- extra-adrenal in 10% (most common site = organ of Zuckerkandl, adjacent to the bifurcation of the aorta)

#### Tests

- 24 hr urinary collection of catecholamines

Surgery is the definitive management. The patient must first however be stabilized with medical management:

- alpha-blocker (e.g. phenoxybenzamine), given before a
- beta-blocker (e.g. propranolol)

A 56-year-old female is admitted to ITU with a severe pneumonia. Thyroid function tests are most likely to show:

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. TSH normal; thyroxine high; T3 high     |
| <input type="radio"/> | B. TSH normal / low; thyroxine low; T3 low |
| <input type="radio"/> | C. TSH high; thyroxine low; T3 low         |
| <input type="radio"/> | D. TSH low; thyroxine high; T3 high        |
| <input type="radio"/> | E. TSH high; thyroxine normal; T3 high     |

Next question

### Sick euthyroid syndrome

In sick euthyroid syndrome (now referred to as non-thyroidal illness) it is often said that everything (TSH, thyroxine and T3) is low. In the majority of cases however the TSH level is within the normal range (inappropriately normal given the low thyroxine and T3).

Changes are reversible upon recovery from the systemic illness.

Which one of the following is the most common non-iatrogenic cause of Cushing's syndrome?

<input type="radio"/>	A. Ectopic ACTH production
<input type="radio"/>	B. Adrenal adenoma
<input type="radio"/>	C. Micronodular adrenal dysplasia
<input type="radio"/>	D. Adrenal carcinoma
<input type="radio"/>	E. Pituitary tumour

Next question

Cushing's disease is the most common, non-iatrogenic, cause of Cushing's syndrome

### Cushing's syndrome: causes

ACTH dependent causes

- Cushing's disease (80%): pituitary tumour secreting ACTH producing adrenal hyperplasia
- ectopic ACTH production (5-10%): e.g. small cell lung cancer

ACTH independent causes

- iatrogenic: steroids
- adrenal adenoma (5-10%)
- adrenal carcinoma (rare)
- Carney complex: syndrome including cardiac myxoma
- micronodular adrenal dysplasia (very rare)

Pseudo-Cushing's

- mimics Cushing's
- often due to alcohol excess or severe depression
- causes false positive dexamethasone suppression test or 24 hr urinary free cortisol
- insulin stress test may be used to differentiate

Which of the following is least recognised as a potential complication of acromegaly?

<input type="radio"/>	A. Colorectal cancer
<input type="radio"/>	B. Hypertension
<input type="radio"/>	C. Cardiomyopathy
<input type="radio"/>	D. Diabetes mellitus
<input type="radio"/>	E. Pulmonary hypertension

Next question

Acromegaly is associated with systemic rather than pulmonary hypertension.

Secondary causes of pulmonary hypertension include COPD, congenital heart disease (Eisenmenger's syndrome), recurrent pulmonary embolism, HIV and sarcoidosis.

### Acromegaly: features

In acromegaly there is excess growth hormone secondary to a pituitary adenoma in over 95% of cases. A minority of cases are caused by ectopic GHRH or GH production by tumours e.g. pancreatic

#### Features

- coarse facial appearance, spade-like hands, increase in shoe size
- large tongue, prognathism, interdental spaces
- excessive sweating and oily skin
- features of pituitary tumour: hypopituitarism, headaches, bitemporal hemianopia
- raised prolactin in 1/3 of cases --> galactorrhoea
- 6% of patients have MEN-1

#### Complications

- hypertension
- diabetes (>10%)
- cardiomyopathy
- colorectal cancer

Each one of the following is a cause of nephrogenic diabetes insipidus, except:

<input type="radio"/>	A. Hypercalcaemia
<input type="radio"/>	B. Demeclocycline
<input type="radio"/>	C. Histiocytosis X
<input type="radio"/>	D. Lithium
<input type="radio"/>	E. Hypokalaemia

Next question

## Diabetes insipidus

Diabetes insipidus (DI) is a condition characterised by either a deficiency of antidiuretic hormone, ADH, (cranial DI) or an insensitivity to antidiuretic hormone (nephrogenic DI).

### Causes of cranial DI

- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X
- DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

### Causes of nephrogenic DI

- genetic: the more common form affects the vasopressin (ADH) receptor, the less common form results from a mutation in the gene that encodes the aquaporin 2 channel
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

### Features

- polyuria
- polydipsia

### Investigation

- high plasma osmolarity, low urine osmolarity
- water deprivation test

The first-line treatment in remnant hyperlipidaemia (dysbetalipoproteinaemia) is:

<input type="radio"/>	A. Ursodeoxycholic acid
<input type="radio"/>	B. Vitamin A
<input type="radio"/>	C. Statins
<input type="radio"/>	D. Fish oil
<input type="radio"/>	E. Fibrates

Next question

## Remnant hyperlipidaemia

### Overview

- rare cause of mixed hyperlipidaemia (raised cholesterol and triglyceride levels)
- also known as Fredrickson type III hyperlipidaemia, broad-beta disease and dysbetalipoproteinaemia
- associated with apo-e2 homozygosity
- high incidence of ischaemic heart disease and peripheral vascular disease
- thought to be caused by impaired removal of intermediate density lipoprotein from the circulation by the liver

### Features

- yellow palmar creases
- palmer xanthomas
- tuberous xanthomas

### Management

- fibrates are first line treatment



**Question 61 of 153**

Next

Liddle's syndrome is associated with each one of the following, except:

<input type="radio"/>	A. Alkalosis
<input type="radio"/>	B. Response to treatment with amiloride
<input type="radio"/>	C. Hypertension
<input type="radio"/>	D. Autosomal recessive inheritance
<input type="radio"/>	E. Hypokalaemia

Next question

**Liddle's syndrome**

Liddle's syndrome is a rare autosomal dominant condition that causes hypertension and hypokalaemic alkalosis. It is thought to be caused by disordered sodium channels in the distal tubules leading to increased reabsorption of sodium.

Treatment is with either amiloride or triamterene

A 62-year-old HGV driver is reviewed. He was diagnosed last year with type 2 diabetes mellitus. Following weight loss and metformin his HbA1c has decreased from 8.8% to 8.4%. What is the most suitable next step in management?

<input type="radio"/>	A. Add exenatide
<input type="radio"/>	B. Make no changes to management
<input type="radio"/>	C. Add gliclazide
<input type="radio"/>	D. Stop metformin for a period to ensure hypoglycaemic awareness is not lost
<input type="radio"/>	E. Add pioglitazone

[Next question](#)

Pioglitazone is the best option here as it would not put him at risk of hypoglycaemia, which obviously could be dangerous given his job. The NICE guidelines would also support the use of a DPP-4 inhibitor (sitagliptin or vildagliptin) in this situation where the risk of hypoglycaemia must be avoided.

### Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

#### Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

#### HbA1c

- the general target for patients is 48 mmol/mol (DCCT = 6.5%). HbA1c levels below 48 mmol/mol (DCCT = 6.5%) should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

#### Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first\*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 48 mmol/mol (DCCT = 6.5%)
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 58 mmol/mol (DCCT = 7.5%) then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% at 6 months)

#### Starting insulin

- usually commenced if HbA1c > 58 mmol/mol (DCCT = 7.5%)
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

#### Other risk factor modification

- current NICE guidelines suggest giving aspirin to all patients > 50 years and to younger patients with other significant risk factors. However, recent evidence does not support this approach. The 2010 SIGN guidelines do not advocate the use of aspirin for primary prevention in diabetics
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reached consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

\*many local protocols now recommend starting metformin upon diagnosis

**Question 63 of 153**

Next

A 36-year-old woman who presented with a goitre is diagnosed with autoimmune thyroiditis. Which one of the following types of thyroid cancer is she predisposed to developing?

- ☐ A. Anaplastic
- ☐ B. Lymphoma
- ☐ C. Medullary
- ☐ D. Follicular
- ☐ E. Papillary

Next question

Hashimoto's thyroiditis is associated with thyroid lymphoma

**Thyroid cancer**

Features of hyperthyroidism or hypothyroidism are not commonly seen in patients with thyroid malignancies as they rarely secrete thyroid hormones

Type	Percentage	
Papillary	70%	Often young females - excellent prognosis
Follicular	20%	
Medullary	5%	Cancer of parafollicular cells, secrete calcitonin, part of MEN-2
Anaplastic	1%	Not responsive to treatment, can cause pressure symptoms
Lymphoma	Rare	Associated with Hashimoto's

Management of papillary and follicular cancer

- total thyroidectomy
- followed by radioiodine (I-131) to kill residual cells
- yearly thyroglobulin levels to detect early recurrent disease

You review a 68-year-old man who has chronic obstructive pulmonary disease (COPD). Each year he typically has around 7-8 courses of oral prednisolone to treat infective exacerbations of his COPD. Which one of the following adverse effects is linked to long-term steroid use?

- ☐ A. Osteomalacia
- ☐ B. Enophthalmos
- ☐ C. Leucopaenia
- ☐ D. Avascular necrosis
- ☐ E. Constipation

Next question

Long-term corticosteroid use is linked to osteopaenia and osteoporosis, rather than osteomalacia.

### Corticosteroids

Corticosteroids are amongst the most commonly prescribed therapies in clinical practice. They are used both systemically (oral or intravenous) or locally (skin creams, inhalers, eye drops, intra-articular). They augment and in some cases replace the natural glucocorticoid and mineralocorticoid activity of endogenous steroids.

The relative glucocorticoid and mineralocorticoid activity of commonly used steroids is shown below:

Minimal glucocorticoid activity, very high mineralocorticoid activity,	Glucocorticoid activity, high mineralocorticoid activity,	Predominant glucocorticoid activity, low mineralocorticoid activity	Very high glucocorticoid activity, minimal mineralocorticoid activity
Fludrocortisone	Hydrocortisone	Prednisolone	Dexamethasone Betmethasone

### Side-effects

The side-effects of corticosteroids are numerous and represent the single greatest limitation on their usage. Side-effects are more common with systemic and prolonged therapy.

#### Glucocorticoid side-effects

- endocrine: impaired glucose regulation, increased appetite/weight gain, hirsutism, hyperlipidaemia
- Cushing's syndrome: moon face, buffalo hump, striae
- musculoskeletal: osteoporosis, proximal myopathy, avascular necrosis of the femoral head
- immunosuppression: increased susceptibility to severe infection, reactivation of tuberculosis
- psychiatric: insomnia, mania, depression
- gastrointestinal: peptic ulceration, acute pancreatitis
- ophthalmic: glaucoma, cataracts

- suppression of growth in children

#### Mineralocorticoid side-effects

- fluid retention
- hypertension

#### Selected points on the use of corticosteroids:

- patients on long-term steroids should have their doses doubled during intercurrent illness
- the BNF suggests gradual withdrawal of systemic corticosteroids if patients have: received more than 40mg prednisolone daily for more than one week, received more than 3 weeks treatment or recently received repeated courses

A 51-year-old woman who is known to have poorly controlled type 1 diabetes mellitus is reviewed. Her main presenting complaint is bloating and vomiting after eating. She also notes that her blood glucose readings have become more erratic recently. Which one of the following medications is most likely to be beneficial?

<input type="radio"/>	A. <i>Helicobacter pylori</i> eradication therapy
<input type="radio"/>	B. Lansoprazole
<input type="radio"/>	C. Amitriptyline
<input type="radio"/>	D. Metoclopramide
<input type="radio"/>	E. Cyclizine

[Next question](#)

### Diabetic neuropathy

NICE updated its guidance on the management of diabetic neuropathy in 2010:

- first-line: oral duloxetine. Oral amitriptyline if duloxetine is contraindicated.
- second-line treatment: if first-line treatment was with duloxetine, switch to amitriptyline or pregabalin, or combine with pregabalin. If first-line treatment was with amitriptyline, switch to or combine with pregabalin
- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

### Gastroparesis

- symptoms include erratic blood glucose control, bloating and vomiting
- management options include metoclopramide, domperidone or erythromycin (prokinetic agents)

Which of the following results establishes a diagnosis of diabetes mellitus?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Asymptomatic patient with fasting glucose 7.9 mmol/L on one occasion |
| <input type="radio"/> | B. Symptomatic patient with fasting glucose 6.8 mmol/L on two occasions |
| <input type="radio"/> | C. Glycosuria +++   |
| <input type="radio"/> | D. Asymptomatic patient with random glucose 22.0 mmol/L on one occasion |
| <input type="radio"/> | E. Symptomatic patient with random glucose 12.0 mmol/L on one occasion  |

Next question

Diabetes diagnosis: fasting > 7.0, random > 11.1 - if asymptomatic need two readings

### Diabetes mellitus: diagnosis

The following is based on the World Health Organisation (WHO) 2006 guidelines.

#### Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

In 2011 WHO released supplementary guidance on the use of HbA1c on the diagnosis of diabetes:

- a HbA1c of greater than or equal to 6.5% (48 mmol/mol) is diagnostic of diabetes mellitus
- a HbA1c value of less than 6.5% does not exclude diabetes (i.e. it is not as sensitive as fasting samples for detecting diabetes)
- in patients without symptoms, the test must be repeated to confirm the diagnosis
- it should be remembered that misleading HbA1c results can be caused by increased red cell turnover (for example anaemia, haemoglobinopathies and pregnancy)

#### Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)



Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

Which one of the following features is not seen in carcinoid syndrome?

<input type="radio"/>	A. Flushing
<input type="radio"/>	B. Diarrhoea
<input type="radio"/>	C. Bronchospasm
<input type="radio"/>	D. Hypertension
<input type="radio"/>	E. Pellagra

Next question

Flushing, diarrhoea, bronchospasm, tricuspid stenosis, pellagra --> carcinoid with liver mets - diagnosis: urinary 5-HIAA

Hypo- not hypertension is seen in carcinoid syndrome secondary to serotonin release

### Carcinoid tumours

#### Carcinoid syndrome

- usually occurs when metastases are present in the liver and release serotonin into the systemic circulation
- may also occur with lung carcinoid as mediators are not 'cleared' by the liver

#### Features

- flushing (often earliest symptom)
- diarrhoea
- bronchospasm
- hypotension
- right heart valvular stenosis (left heart can be affected in bronchial carcinoid)
- other molecules such as ACTH and GHRH may also be secreted resulting in, for example, Cushing's syndrome
- pellagra can rarely develop as dietary tryptophan is diverted to serotonin by the tumour

#### Investigation

- urinary 5-HIAA
- plasma chromogranin A y

#### Management

- somatostatin analogues e.g. octreotide
- diarrhoea: cyproheptadine may help

Which one of the following statements regarding impaired glucose regulation is correct?

- ☐ A. All patient should have a repeat oral glucose tolerance test every 2 years
- ☐ B. Patients with impaired glucose tolerance are more likely to develop diabetes than patients with impaired fasting glycaemia
- ☐ C. Impaired glucose tolerance (IGT) is defined as a fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l
- ☐ D. Around 1 in 20 adults in the UK have impaired glucose regulation
- ☐ E. Patients should be offered metformin if lifestyle changes fail to improve their glucose profile

Next question

### Impaired glucose regulation

Impaired glucose regulation (IGR) may also be referred to as non-diabetic hyperglycaemia (NDH) or prediabetes. It describes blood glucose levels which are above the normal range but not high enough for a diagnosis of diabetes mellitus. Diabetes UK estimate that around 1 in 7 adults in the UK have IGR. Many individuals with IGR will progress on to developing type 2 diabetes mellitus (T2DM) and they are therefore at greater risk of microvascular and macrovascular complications.

There are two main types of IGR:

- impaired fasting glucose (IFG) - due to hepatic insulin resistance
- impaired glucose tolerance (IGT) - due to muscle insulin resistance
- patients with IGT are more likely to develop T2DM and cardiovascular disease than patients with IFG

### Definitions

- a fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)
- impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l
- the role of HbA1c in diagnosing IGR and diabetes is currently under review
- people with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT

### Management

- Diabetes UK suggests using the term 'prediabetes' when discussing the condition with patients as research has shown that this term has the most impact and is most easily understood
- lifestyle modification: weight loss, increased exercise, change in diet
- drug therapy is not currently licensed or recommended for patients with IGR in the UK
- at least yearly follow-up with blood tests is recommended

**Question 69 of 153**

Next

A 47-year-old woman is referred to the general medical clinic. She has gained 10 kg in weight in the past 3 months but her main problem is episodic sweating. These episodes of sweating are associated with double vision and typically occur early in the morning. Clinical examination is unremarkable. What is the most likely diagnosis?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Bronchial carcinoid     |
| <input type="radio"/> | B. Hashimoto's thyroiditis |
| <input type="radio"/> | C. Menopause               |
| <input type="radio"/> | D. Cushing's syndrome      |
| <input type="radio"/> | E. Insulinoma              |

Next question

This is a typical presentation of insulinoma

**Insulinoma**

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

**Basics**

- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

**Features**

- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

**Diagnosis**

- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

**Management**

- surgery
- diazoxide and somatostatin if patients are not candidates for surgery

Which one of the following features of haemochromatosis may be reversible with treatment?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Cardiomyopathy                 |
| <input type="radio"/> | B. Hypogonadotrophic hypogonadism |
| <input type="radio"/> | C. Diabetes mellitus              |
| <input type="radio"/> | D. Arthropathy                    |
| <input type="radio"/> | E. Liver cirrhosis                |

Next question

### Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6\*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

#### Epidemiology

- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

#### Presenting features

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	Irreversible complications
<ul style="list-style-type: none"> <li>• Cardiomyopathy</li> <li>• Skin pigmentation</li> </ul>	<ul style="list-style-type: none"> <li>• Liver cirrhosis**</li> <li>• Diabetes mellitus</li> <li>• Hypogonadotrophic hypogonadism</li> <li>• Arthropathy</li> </ul>

\*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

\*\*whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not

Each one of the following is associated with pseudohypoparathyroidism, except:

<input type="radio"/>	A. Low calcium levels
<input type="radio"/>	B. Low PTH levels
<input type="radio"/>	C. Shortened 4th and 5th metacarpals
<input type="radio"/>	D. Low IQ
<input type="radio"/>	E. Short stature

Next question

## Hypoparathyroidism

### Primary hypoparathyroidism

- decrease PTH secretion
- e.g. secondary to thyroid surgery
- low calcium, high phosphate
- treated with alfacalcidol

The main symptoms of hypoparathyroidism are secondary to hypocalcaemia:

- tetany: muscle twitching, cramping and spasm
- perioral paraesthesia
- Trousseau's sign: carpal spasm if the brachial artery occluded by inflating the blood pressure cuff and maintaining pressure above systolic
- Chvostek's sign: tapping over parotid causes facial muscles to twitch
- if chronic: depression, cataracts
- ECG: prolonged QT interval

### Pseudohypoparathyroidism

- target cells being insensitive to PTH
- due to abnormality in a G protein
- associated with low IQ, short stature, shortened 4th and 5th metacarpals
- low calcium, high phosphate, high PTH
- diagnosis is made by measuring urinary cAMP and phosphate levels following an infusion of PTH. In hypoparathyroidism this will cause an increase in both cAMP and phosphate levels. In pseudohypoparathyroidism type I neither cAMP nor phosphate levels are increased whilst in pseudohypoparathyroidism type II only cAMP rises.

### Pseudopseudohypoparathyroidism

- similar phenotype to pseudohypoparathyroidism but normal biochemistry



Which one of the following skin disorders is least associated with hypothyroidism?

<input type="radio"/>	A. Xanthomata
<input type="radio"/>	B. Pruritus
<input type="radio"/>	C. Pretibial myxoedema
<input type="radio"/>	D. Eczema
<input type="radio"/>	E. Dry, coarse hair

Next question

For the purposes of postgraduate exams pretibial myxoedema is associated with thyrotoxicosis. There are however case reports of it been found in hypothyroid patients, especially the diffuse non-pitting variety

### Skin disorders associated with thyroid disease

Skin manifestations of hypothyroidism

- dry (anhydrosis), cold, yellowish skin
- non-pitting oedema (e.g. hands, face)
- dry, coarse scalp hair, loss of lateral aspect of eyebrows
- eczema
- xanthomata

Skin manifestations of hyperthyroidism

- pretibial myxoedema: erythematous, oedematous lesions above the lateral malleoli
- thyroid acropachy: clubbing
- scalp hair thinning
- increased sweating

Pruritus can occur in both hyper- and hypothyroidism

Cushing's syndrome is most typically associated with which one of the following abnormalities:

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Hypokalaemic metabolic acidosis   |
| <input type="radio"/> | B. Hyperkalaemic metabolic alkalosis |
| <input type="radio"/> | C. Hypocalcaemic metabolic acidosis  |
| <input type="radio"/> | D. Hypokalaemic metabolic alkalosis  |
| <input type="radio"/> | E. Hyperkalaemic metabolic acidosis  |

Next question

Cushing's syndrome - hypokalaemic metabolic alkalosis

### Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

### Tests to confirm Cushing's syndrome

The two most commonly used tests are:

- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

### Localisation tests

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test

- if pituitary source then cortisol suppressed
- if ectopic/adrenal then no change in cortisol

CRH stimulation

- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

An insulin stress test is most useful in the investigation of:

<input type="radio"/>	A. Glucagonoma
<input type="radio"/>	B. Insulinoma
<input type="radio"/>	C. Addison's disease
<input type="radio"/>	D. Hypopituitarism
<input type="radio"/>	E. Diabetes mellitus

Next question

Insulin stress tests are also occasionally used to differentiate Cushing's from pseudo-Cushing's

### Insulin stress test

#### Basics

- used in investigation of hypopituitarism
- IV insulin given, GH and cortisol levels measured
- with normal pituitary function GH and cortisol should rise

#### Contraindications

- epilepsy
- ischaemic heart disease
- adrenal insufficiency

A 34-year-old female with a history of Addison's disease presents for review in endocrinology clinic. She is generally well but complains of a decrease in her libido. On examination there is a slight loss of pubic hair. What is the most likely cause?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Adverse effect of hydrocortisone therapy |
| <input type="radio"/> | B. 11-hydroxylase deficiency                |
| <input type="radio"/> | C. Diethylstilbestrol deficiency            |
| <input type="radio"/> | D. Oestrogen deficiency                     |
| <input type="radio"/> | E. Dehydroepiandrosterone (DHEA) deficiency |

[Next question](#)

Dehydroepiandrosterone is the most abundant circulating adrenal steroid. Adrenal glands are the main source of dehydroepiandrosterone in females - loss of functioning adrenal tissue as in Addison's disease may result in symptoms secondary to androgen deficiency, such as loss of libido. Research is ongoing as to whether routine replacement of DHEA is beneficial

### Addison's disease

Autoimmune destruction of the adrenal glands is the commonest cause of hypoadrenalism in the UK, accounting for 80% of cases

#### Features

- lethargy, weakness, anorexia, nausea & vomiting, weight loss
- hyperpigmentation, vitiligo, loss of pubic hair in women
- crisis: collapse, shock, pyrexia

### Other causes of hypoadrenalism

#### Primary causes

- tuberculosis
- metastases (e.g. bronchial carcinoma)
- meningococcal septicaemia (Waterhouse-Friderichsen syndrome)
- HIV
- antiphospholipid syndrome

#### Secondary causes

- pituitary disorders (e.g. tumours, irradiation, infiltration)

#### Exogenous glucocorticoid therapy

**Question 76 of 153**[Next](#)

A 44-year-old woman presents to her GP as she is feeling 'hot all the time' and is consequently worried she is going through an early menopause. Her husband has also noticed a 'fullness' of her neck which has become apparent over the past few weeks. On examination her pulse is 90/minute and she has a small, non-tender goitre. Blood tests are arranged:

TSH	< 0.05 mu/l
Free T4	24 pmol/l
Anti-thyroid peroxidase antibodies	102 IU/mL (< 35 IU/mL)
ESR	23 mm/hr

What is the most likely diagnosis?

- ☐ A. Hashimoto's thyroiditis
- ☐ B. Toxic multinodular goitre
- ☐ C. Thyroid cancer
- ☐ D. De Quervain's thyroiditis
- ☐ E. Graves' disease

[Next question](#)

The thyrotoxic symptoms and blood tests, goitre and anti-thyroid peroxidase antibodies suggest a diagnosis of Graves' disease.

The ESR result is within normal range.

Hashimoto's thyroiditis is associated with hypothyroidism.

**Graves' disease: features**

Graves' disease is the most common cause of thyrotoxicosis. It is typically seen in women aged 30-50 years.

**Features**

- typical features of thyrotoxicosis
- specific signs limited to Grave's (see below)

Features seen in Graves' but not in other causes of thyrotoxicosis

- eye signs (30% of patients): exophthalmos, ophthalmoplegia
- pretibial myxoedema
- thyroid acropachy

## Autoantibodies

- anti-TSH receptor stimulating antibodies (90%)
- anti-thyroid peroxidase antibodies (50%)

A 53-year-old female with a history of primary atrophic hypothyroidism is assessed two months following a change in her dose of levothyroxine. Which one of the following best describes what the TSH should ideally be?

<input type="radio"/>	A. Between 0.5 to 1.0 mU/l
<input type="radio"/>	B. Between 0.5 to 2.5 mU/l
<input type="radio"/>	C. Between 2.5 to 4.5 mU/l
<input type="radio"/>	D. Between 1.5 to 3.5 mU/l
<input type="radio"/>	E. Between 3.5 to 5.5 mU/l

[Next question](#)

A TSH value between 0.5 to 2.5 mU/l is now considered preferable. Dosage changes should of course also take account of symptoms

### Hypothyroidism: management

#### Key points

- initial starting dose of levothyroxine should be lower in elderly patients and those with ischaemic heart disease (e.g. 25-50 mcg/day)
- following a change in thyroxine dose thyroid function tests should be checked after 6-8 weeks
- the therapeutic goal is 'normalisation' of the thyroid stimulating hormone (TSH) level. As the majority unaffected people have a TSH value 0.5-2.5 mU/l it is now thought preferable to aim for a TSH in this range
- there is no evidence to support combination therapy with levothyroxine and liothyronine

#### Side-effects of thyroxine therapy

- hyperthyroidism: due to over treatment
- reduced bone mineral density
- worsening of angina
- atrial fibrillation

#### Interactions

- iron: absorption of levothyroxine reduced, give at least 2 hours apart



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Next

A 69-year-old man who had a stroke 6 months ago is reviewed. After his diagnosis he was started on simvastatin 40mg on for secondary prevention of further cardiovascular disease. A fasting lipid profile taken one week ago is reported as follows:

Total cholesterol	5.4 mmol/l
HDL cholesterol	1.0 mmol/l
LDL cholesterol	4.1 mmol/l
Triglyceride	1.5 mmol/l

According to recent NICE guidelines, what is the most appropriate action?

- ☐ A. Switch to simvastatin 80mg on
- ☐ B. No change in medication, repeat lipid profile in 6 months
- ☐ C. Add nicotinic acid
- ☐ D. Switch to atorvastatin 80mg on
- ☐ E. Add ezetimibe

Next question

Nicotinic acid can raise HDL levels by up to 30% but in practice its use is limited by flushing. Any change to treatment should of course be in conjunction with continued lifestyle advice.

The increased risk of myopathy with the 80mg dose of simvastatin was recently highlighted by the Medicines and Healthcare products Regulatory Agency. Please see the link for more details.

**Hyperlipidaemia: management**

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

**Primary prevention**

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

NICE updated their lipid guidelines so that the following risk models are valid:

- Framingham
- Joint British Society 2 (JBS2)
- QRISK
- ASSIGN (Scotland only)

The 1991 Framingham equations may still be used. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- males of South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be checked at baseline, within 3 months and at 12 months but not again unless clinically indicated

## **Secondary prevention**

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing simvastatin to 80mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained.

A 22-year-old female presents with recurrent painful oral ulceration. Examination reveals signs of oral *Candidal* infection. Which one of the following would most suggest type 1 polyglandular syndrome?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Hypocalcaemia             |
| <input type="radio"/> | B. Rheumatoid arthritis      |
| <input type="radio"/> | C. Type II diabetes mellitus |
| <input type="radio"/> | D. Coeliac disease           |
| <input type="radio"/> | E. Hypercalcaemia            |

[Next question](#)

Primary hypoparathyroidism is usually the first endocrine manifestation of type 1 autoimmune polyendocrinopathy syndrome. The contrast to multiple endocrine neoplasia (MEN), where hyperparathyroidism is a common finding, should be noted

The question gives a slightly atypical history as this is the upper end of the age range in which patients would be expected to present

### Autoimmune polyendocrinopathy syndrome

Addison's disease (autoimmune hypoadrenalism) is associated with other endocrine deficiencies in approximately 10% of patients. There are two distinct types of autoimmune polyendocrinopathy syndrome (APS), with type 2 (sometimes referred to as Schmidt's syndrome) being much more common.

APS type 2 has a polygenic inheritance and is linked to HLA DR3/DR4. Patients have Addison's disease plus either:

- type 1 diabetes mellitus
- autoimmune thyroid disease

APS type 1 is occasionally referred to as Multiple Endocrine Deficiency Autoimmune Candidiasis (MEDAC). It is a very rare autosomal recessive disorder caused by mutation of AIRE1 gene on chromosome 21

Features of APS type 1 (2 out of 3 needed)

- chronic mucocutaneous candidiasis (typically first feature as young child)
- Addison's disease
- primary hypoparathyroidism

Vitiligo can occur in both types

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Next

A 23-year-old woman presents for review. She has not a normal period for around 8 months now. A recent pregnancy test was negative. Blood tests are ordered:

FSH	2.2 IU/L (0-20 IU/L)
Oestradiol	84 pmol/l (100-500 pmol/l)
Thyroid stimulating hormone	3.1 mIU/L
Prolactin	2 ng/ml (0-10 ng/ml)
Free androgen index	3 ( < 7 )

What is the most likely cause of her symptoms?

- ☐ A. Prolactinoma
- ☐ B. Premature ovarian failure
- ☐ C. Polycystic ovarian syndrome
- ☐ D. Addison's disease
- ☐ E. Excessive exercise

Next question

The bloods show a hypothalamic amenorrhoea which may be caused by stress or excessive exercise. The FSH would be raised in premature ovarian failure.

**Amenorrhoea**

Amenorrhoea may be divided into primary (failure to start menses by the age of 16 years) or secondary (cessation of established, regular menstruation for 6 months or longer).

Causes of primary amenorrhoea

- Turner's syndrome
- testicular feminisation
- congenital adrenal hyperplasia
- congenital malformations of the genital tract

Causes of secondary amenorrhoea (after excluding pregnancy)

- hypothalamic amenorrhoea (e.g. Stress, excessive exercise)
- polycystic ovarian syndrome (PCOS)
- hyperprolactinaemia
- premature ovarian failure
- thyrotoxicosis\*

## Initial investigations

- exclude pregnancy with urinary or serum bHCG
- gonadotrophins: low levels indicate a hypothalamic cause where as raised levels suggest an ovarian problem (e.g. Premature ovarian failure)
- prolactin
- androgen levels: raised levels may be seen in PCOS
- oestradiol
- thyroid function tests

\*hypothyroidism may also cause amenorrhoea

A 54-year-old man with type 2 diabetes mellitus is found on annual review to have new vessel formation at the optic disc. Visual acuity in both eyes is not affected (6/9). Blood pressure is 155/84 mmHg.

HbA1c	8.4%
-------	------

What is the most important intervention in this patient?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Follow-up ophthalmoscopy in 3 months |
| <input type="radio"/> | B. Add aspirin                          |
| <input type="radio"/> | C. Blood pressure control               |
| <input type="radio"/> | D. Tight glycaemic control              |
| <input type="radio"/> | E. Laser therapy                        |

Next question

This patient has proliferative diabetic retinopathy and urgent referral to an ophthalmologist for panretinal photocoagulation is indicated

### Diabetic retinopathy

Diabetic retinopathy is the most common cause of blindness in adults aged 35-65 years-old. Hyperglycaemia is thought to cause increased retinal blood flow and abnormal metabolism in the retinal vessel walls. This precipitates damage to endothelial cells and pericytes

Endothelial dysfunction leads to increased vascular permeability which causes the characteristic exudates seen on fundoscopy. Pericyte dysfunction predisposes to the formation of microaneurysms. Neovascularization is thought to be caused by the production of growth factors in response to retinal ischaemia

In exams you are most likely to be asked about the characteristic features of the various stages/types of diabetic retinopathy. Recently a new classification system has been proposed, dividing patients into those with non-proliferative diabetic retinopathy (NPDR) and those with proliferative retinopathy (PDR):

Traditional classification	New classification
Background retinopathy <ul style="list-style-type: none"> <li>microaneurysms (dots)</li> <li>blot haemorrhages (<math>\leq 3</math>)</li> <li>hard exudates</li> </ul>	Mild NPDR <ul style="list-style-type: none"> <li>1 or more microaneurysm</li> </ul> Moderate NPDR
Pre-proliferative retinopathy <ul style="list-style-type: none"> <li>cotton wool spots (soft exudates;</li> </ul>	<ul style="list-style-type: none"> <li>microaneurysms</li> <li>blot haemorrhages</li> <li>hard exudates</li> </ul>

<p>ischaemic nerve fibres)</p> <ul style="list-style-type: none"> <li>• &gt; 3 blot haemorrhages</li> <li>• venous beading/looping</li> <li>• deep/dark cluster haemorrhages</li> <li>• more common in Type I DM, treat with laser photocoagulation</li> </ul>	<ul style="list-style-type: none"> <li>• cotton wool spots, venous beading/looping and intraretinal microvascular abnormalities (IRMA) less severe than in severe NPDR</li> </ul> <p>Severe NPDR</p> <ul style="list-style-type: none"> <li>• blot haemorrhages and microaneurysms in 4 quadrants</li> <li>• venous beading in at least 2 quadrants</li> <li>• IRMA in at least 1 quadrant</li> </ul>
--	---

### Proliferative retinopathy

- retinal neovascularisation - may lead to vitreous haemorrhage
- fibrous tissue forming anterior to retinal disc
- more common in Type I DM, 50% blind in 5 years

### Maculopathy

- based on location rather than severity, anything is potentially serious
- hard exudates and other 'background' changes on macula
- check visual acuity
- more common in Type II DM

A 64-year-old patient is prescribed pegvisomant for the treatment of acromegaly. What is the mechanism of action of pegvisomant?

<input type="radio"/>	A. IGF-1 receptor antagonist
<input type="radio"/>	B. Growth hormone receptor antagonist
<input type="radio"/>	C. IGF-1 receptor agonist
<input type="radio"/>	D. Growth hormone receptor agonist
<input type="radio"/>	E. Long-acting somatostatin analogue

[Next question](#)

### Acromegaly: management

Trans-sphenoidal surgery is first-line treatment for acromegaly in the majority of patients

Dopamine agonists

- for example bromocriptine
- the first effective medical treatment for acromegaly, however now superseded by somatostatin analogues
- effective only in a minority of patients

Somatostatin analogue

- for example octreotide
- effective in 50-70% of patients
- may be used as an adjunct to surgery

Pegvisomant

- GH receptor antagonist - prevents dimerization of the GH receptor
- once daily s/c administration
- very effective - decreases IGF-1 levels in 90% of patients to normal
- doesn't reduce tumour volume therefore surgery still needed if mass effect

External irradiation is sometimes used for older patients or following failed surgical/medical treatment



Which one of the following is most likely to be seen in a patient with multiple endocrine neoplasia (MEN) type I?

- ☐ A. Pheochromocytoma
- ☐ B. Insulinoma
- ☐ C. Marfanoid body habitus
- ☐ D. Medullary thyroid carcinoma
- ☐ E. RET gene

[Next question](#)

### Multiple endocrine neoplasia

The table below summarises the three main types of multiple endocrine neoplasia (MEN)

MEN type I	MEN type IIa	MEN type IIb
<p>Mnemonic 'three P's':</p> <p>parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia</p> <p>pituitary (70%)</p> <p>pancreas (50%, e.g. insulinoma, gastrinoma)</p> <p>also: adrenal and thyroid</p>	<p>phaeochromocytoma</p> <p>medullary thyroid cancer (70%)</p> <p>parathyroid (60%)</p>	<p>medullary thyroid cancer</p> <p>phaeochromocytoma</p> <p>marfanoid body habitus</p> <p>neuromas</p>
<p>MEN1 gene</p> <p>Most common presentation = hypercalcaemia</p>	<p>RET oncogene</p>	<p>RET oncogene</p>

MEN is inherited as an autosomal dominant disorder

Which one of the following may be associated with galactorrhoea?

<input type="radio"/>	A. Primary hypothyroidism
<input type="radio"/>	B. Addison's disease
<input type="radio"/>	C. Cushing's syndrome
<input type="radio"/>	D. Grave's disease
<input type="radio"/>	E. Bromocriptine

Next question

### Prolactin and galactorrhoea

Prolactin is secreted by the anterior pituitary gland with release being controlled by a wide variety of physiological factors. Dopamine acts as the primary prolactin releasing inhibitory factor and hence dopamine agonists such as bromocriptine may be used to control galactorrhoea. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Features of excess prolactin

- men: impotence, loss of libido, galactorrhoea
- women: amenorrhoea, galactorrhoea

Causes of raised prolactin

- prolactinoma
- pregnancy
- oestrogens
- physiological: stress, exercise, sleep
- acromegaly: 1/3 of patients
- polycystic ovarian syndrome
- primary hypothyroidism (due to thyrotrophin releasing hormone (TRH) stimulating prolactin release)

Drug causes of raised prolactin

- metoclopramide, domperidone
- phenothiazines
- haloperidol
- very rare: SSRIs, opioids

Which one of the following statements regarding polycystic ovarian syndrome (PCOS) is incorrect?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. A slightly elevated prolactin is consistent with a diagnosis of PCOS |
| <input type="radio"/> | B. Luteinizing hormone levels are usually raised                        |
| <input type="radio"/> | C. Hyperinsulinaemia is seen  |
| <input type="radio"/> | D. Acanthosis nigricans may be seen                                     |
| <input type="radio"/> | E. Affects between 2-3% of women of reproductive age                    |

Next question

Polycystic ovarian syndrome is extremely common, affecting between 5-20% of women of reproductive age

### Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome.

#### Features

- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsutism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

#### Investigations

- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful in diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

A 26-year-old obese female is investigated for menstrual disturbance. A diagnosis of polycystic ovarian syndrome is made. Which of the following findings is most consistently seen in polycystic ovarian syndrome?

<input type="radio"/>	A. Obesity
<input type="radio"/>	B. Hirsutism
<input type="radio"/>	C. Ovarian cysts on ultrasound
<input type="radio"/>	D. Raised LH:FSH ratio
<input type="radio"/>	E. Clitoromegaly

[Next question](#)

Polycystic ovarian syndrome - ovarian cysts are the most consistent feature

Whilst all of the features listed above may be seen in polycystic ovarian syndrome, ovarian cysts are the most consistent feature.

### Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome.

#### Features

- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsutism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

#### Investigations

- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful in diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

A 52-year-old man has a set of fasting bloods as part of a work-up for hypertension. The fasting glucose comes back as 6.5 mmol/l. The test is repeated and reported as 6.7 mmol/l. He says he feels constantly tired but denies any polyuria or polydipsia. How should these results be interpreted?

<input type="radio"/>	A. Impaired fasting glycaemia
<input type="radio"/>	B. Suggestive of diabetes mellitus but not diagnostic
<input type="radio"/>	C. Diabetes mellitus
<input type="radio"/>	D. Normal
<input type="radio"/>	E. Impaired glucose tolerance

[Next question](#)

### Diabetes mellitus: diagnosis

The following is based on the World Health Organisation (WHO) 2006 guidelines.

#### Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

In 2011 WHO released supplementary guidance on the use of HbA1c on the diagnosis of diabetes:

- a HbA1c of greater than or equal to 6.5% (48 mmol/mol) is diagnostic of diabetes mellitus
- a HbA1c value of less than 6.5% does not exclude diabetes (i.e. it is not as sensitive as fasting samples for detecting diabetes)
- in patients without symptoms, the test must be repeated to confirm the diagnosis
- it should be remembered that misleading HbA1c results can be caused by increased red cell turnover (for example anaemia, haemoglobinopathies and pregnancy)

#### Impaired fasting glucose and impaired glucose tolerance

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

A 54-year-old female presents to the Emergency Department concerned about double vision. She is noted to have exophthalmos and conjunctival oedema on examination and a diagnosis of thyroid eye disease is suspected. What can be said regarding her thyroid status?

<input type="radio"/>	A. Hyper- or euthyroid
<input type="radio"/>	B. Hypothyroid
<input type="radio"/>	C. Hyperthyroid
<input type="radio"/>	D. Hypo- or euthyroid
<input type="radio"/>	E. Eu-, hypo- or hyperthyroid

[Next question](#)

### Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

#### Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

#### Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

#### Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Dynamic pituitary function tests may be used to assess each one of the following, except:

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Cortisol                       |
| <input type="radio"/> | B. Prolactin                      |
| <input type="radio"/> | C. Growth hormone                 |
| <input type="radio"/> | D. Follicular stimulating hormone |
| <input type="radio"/> | E. Antidiuretic hormone           |

Next question

### Dynamic pituitary function tests

A dynamic pituitary function test is used to assess patients with suspected primary pituitary dysfunction

Insulin, TRH and LHRH are given to the patient following which the serum glucose, cortisol, growth hormone, TSH, LH and FSH levels are recorded at regular intervals. Prolactin levels are also sometimes measured\*

A normal dynamic pituitary function test has the following characteristics:

- GH level rises > 20mu/l
- cortisol level rises > 550 mmol/l
- TSH level rises by > 2 mu/l from baseline level
- LH and FSH should double

\*dopamine antagonist tests using metoclopramide may also be used in the investigation of hyperprolactinaemia. A normal response is at least a twofold rise in prolactin. A blunted prolactin response suggests a prolactinoma



**Question 90 of 153**

Next

A 35-year-old female is referred to the endocrine clinic due to weight loss and palpitations. The following results are obtained:

TSH	< 0.05 mu/l
T4	178 mmol/l

Which one of the following features would most suggest a diagnosis of Grave's disease?

- ☐ A. Atrial fibrillation
- ☐ B. Lid lag
- ☐ C. Family history of radioiodine treatment
- ☐ D. Pretibial myxoedema
- ☐ E. Multinodular goitre

Next question

Pretibial myxoedema is not seen in other causes of thyrotoxicosis and points towards a diagnosis of Graves'

**Graves' disease: features**

Graves' disease is the most common cause of thyrotoxicosis. It is typically seen in women aged 30-50 years.

**Features**

- typical features of thyrotoxicosis
- specific signs limited to Grave's (see below)

**Features seen in Graves' but not in other causes of thyrotoxicosis**

- eye signs (30% of patients): exophthalmos, ophthalmoplegia
- pretibial myxoedema
- thyroid acropachy

**Autoantibodies**

- anti-TSH receptor stimulating antibodies (90%)
- anti-thyroid peroxidase antibodies (50%)

Which one of the following is the most common cause of hypothyroidism in the UK?

<input type="radio"/>	A. Pituitary failure
<input type="radio"/>	B. Dietary iodine deficiency
<input type="radio"/>	C. Lithium therapy
<input type="radio"/>	D. Primary atrophic hypothyroidism
<input type="radio"/>	E. Hashimoto's thyroiditis

Next question

In European countries primary atrophic hypothyroidism is the most cause causes of hypothyroidism, whereas in North America Hashimoto's thyroiditis appears to account for the majority of cases. The reason for this discrepancy is unclear

### Hypothyroidism: causes

Hypothyroidism affects around 1-2% of women in the UK and is around 5-10 times more common in females than males.

#### Primary hypothyroidism

Primary atrophic hypothyroidism

- most common cause
- autoimmune disease, associated with IDDM, Addison's or pernicious anaemia
- 5 times more common in women

Hashimoto's thyroiditis

- autoimmune disease as above with goitre (positive microsomal antibodies)
- may cause transient thyrotoxicosis in the acute phase
- 10 times more common in women

After thyroidectomy or radioiodine treatment

Drug therapy (e.g. lithium, amiodarone or anti-thyroid drugs such as carbimazole)

Dietary iodine deficiency

#### Secondary hypothyroidism (rare)

From pituitary failure

Other associated conditions

- Down's syndrome
- Turner's syndrome
- coeliac disease

Each one of the following is a cause of cranial diabetes insipidus, except:

<input type="radio"/>	A. Pituitary surgery
<input type="radio"/>	B. Lithium
<input type="radio"/>	C. Histiocytosis X
<input type="radio"/>	D. Craniopharyngioma
<input type="radio"/>	E. Post head-injury

[Next question](#)

Lithium causes a nephrogenic diabetes insipidus

### Diabetes insipidus

Diabetes insipidus (DI) is a condition characterised by either a deficiency of antidiuretic hormone, ADH, (cranial DI) or an insensitivity to antidiuretic hormone (nephrogenic DI).

#### Causes of cranial DI

- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X
- DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

#### Causes of nephrogenic DI

- genetic: the more common form affects the vasopressin (ADH) receptor, the less common form results from a mutation in the gene that encodes the aquaporin 2 channel
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

#### Features

- polyuria
- polydipsia

#### Investigation

- high plasma osmolarity, low urine osmolarity
- water deprivation test

What is the most common cause of primary hyperaldosteronism?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Pituitary tumour                         |
| <input type="radio"/> | B. Adrenocortical adenoma                   |
| <input type="radio"/> | C. Adrenal carcinoma                        |
| <input type="radio"/> | D. Ectopic secretion                        |
| <input type="radio"/> | E. Bilateral idiopathic adrenal hyperplasia |

Next question

Bilateral idiopathic adrenal hyperplasia is the most common cause of primary hyperaldosteronism

### Primary hyperaldosteronism

Primary hyperaldosteronism was previously thought to be most commonly caused by an adrenal adenoma, termed Conn's syndrome. However, recent studies have shown that bilateral idiopathic adrenal hyperplasia is the cause in up to 70% of cases. Differentiating between the two is important as this determines treatment. Adrenal carcinoma is an extremely rare cause of primary hyperaldosteronism

#### Features

- hypertension
- hypokalaemia (e.g. muscle weakness)
- alkalosis

#### Investigations

- high serum aldosterone
- low serum renin
- high-resolution CT abdomen

#### Management

- adrenal adenoma: surgery
- bilateral adrenocortical hyperplasia: aldosterone antagonist e.g. spironolactone

\*please note that some of these notes have been copied to Wikipedia, and not vice-versa

A 45-year woman who you have treated for obesity comes for review. Despite ongoing lifestyle interventions and trials of orlistat and sibutramine she has failed to lose a significant amount of weight. She is currently taking ramipril for hypertension but a recent fasting glucose was normal. For this patient, what is the cut-off body mass index (BMI) that would trigger a referral for consideration of bariatric surgery?

- ☐ A. BMI > 35 kg/m<sup>2</sup>
- ☐ B. BMI > 40 kg/m<sup>2</sup>
- ☐ C. BMI > 30 kg/m<sup>2</sup>
- ☐ D. BMI > 38 kg/m<sup>2</sup>
- ☐ E. BMI > 45 kg/m<sup>2</sup>

[Next question](#)

#### Obesity - NICE bariatric referral cut-offs

- with risk factors (T2DM, BP etc): > 35 kg/m<sup>2</sup>
- no risk factors: > 40 kg/m<sup>2</sup>

### Obesity: bariatric surgery

The use of bariatric surgery in the management of obesity has developed significantly over the past decade. It is now recognised that for many obese patients who fail to lose weight with lifestyle and drug interventions the risks and expense of long-term obesity outweigh those of surgery.

#### NICE guidelines on bariatric surgery for adults

Consider surgery for people with severe obesity if:

- they have a BMI of 40 kg/m<sup>2</sup> or more, or between 35 kg/m<sup>2</sup> and 40 kg/m<sup>2</sup> and other significant disease (for example, type 2 diabetes mellitus, hypertension) that could be improved if they lost weight
- all appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- they are receiving or will receive intensive specialist management
- they are generally fit for anaesthesia and surgery
- they commit to the need for long-term follow-up

Consider surgery as a first-line option for adults with a BMI of more than 50 kg/m<sup>2</sup> in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long

Types of bariatric surgery:

- primarily restrictive: laparoscopic-adjustable gastric banding (LAGB) or sleeve gastrectomy
- primarily malabsorptive: classic biliopancreatic diversion (BPD) has now largely been replaced by biliopancreatic diversion with duodenal switch
- mixed: Roux-en-Y gastric bypass surgery

Which operation?

- LAGB produces less weight loss than malabsorptive or mixed procedures but as it has fewer complications it is normally the first-line intervention in patients with a BMI of 30-39kg/m<sup>2</sup>
- patients with a BMI > 40 kg/m<sup>2</sup> may be considered for a gastric bypass or sleeve gastrectomy. The latter may be done as a sole procedure or as an initial procedure prior to bypass
- primarily malabsorptive procedures are usually reserved for very obese patients (e.g. BMI > 60 kg/m<sup>2</sup>)

Which one of the following features is least commonly seen in Gitelman's syndrome?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Hypokalaemia        |
| <input type="radio"/> | B. Hypertension        |
| <input type="radio"/> | C. Metabolic alkalosis |
| <input type="radio"/> | D. Hypocalciuria       |
| <input type="radio"/> | E. Hypomagnesaemia     |

Next question

Gitelman's syndrome: normotension with hypokalaemia

### Gitelman's syndrome

Gitelman's syndrome is due to a defect in the thiazide-sensitive  $\text{Na}^+ \text{Cl}^-$  transporter in the distal convoluted tubule.

#### Features

- hypokalaemia
- hypomagnesaemia
- hypocalciuria
- metabolic alkalosis
- normotension



A 54-year-old man with type 2 diabetes mellitus is started on exenatide. Which one of the following statements regarding exenatide is incorrect?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Typically results in weight loss              |
| <input type="radio"/> | B. May be combined with a sulfonylurea           |
| <input type="radio"/> | C. The major adverse effect is flu-like symptoms |
| <input type="radio"/> | D. Should be given twice a day                   |
| <input type="radio"/> | E. Must be given by subcutaneous injection       |

Next question

Exenatide causes vomiting

The major adverse effect is nausea and vomiting

### Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HbA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

**Question 97 of 153**

Next

A 52-year-old woman who was diagnosed as having primary atrophic hypothyroidism 12 months ago is reviewed following recent thyroid function tests (TFTs):

TSH	12.5 mU/l
Free T4	14 pmol/l

She is currently taking 75mcg of levothyroxine once a day. How should these results be interpreted?

- ☐ A. Poor compliance with medication
- ☐ B. Taking extra thyroxine
- ☐ C. Evidence of recent systemic steroid therapy
- ☐ D. Keep on same dose
- ☐ E. T4 to T3 conversion disorder

Next question

**Thyroid function tests**

The interpretation of thyroid function tests is usually straightforward:

	TSH	Free T4	
Thyrotoxicosis (e.g. Graves' disease)	Low	High	In T3 thyrotoxicosis the free T4 will be normal
Primary hypothyroidism (primary atrophic hypothyroidism)	High	Low	
Secondary hypothyroidism	Low	Low	Replacement steroid therapy is required prior to thyroxine
Sick euthyroid syndrome*	Low**	Low	Common in hospital inpatients
Poor compliance with thyroxine	High	Normal / high	
Steroid therapy	Low	Normal	

\*now referred to as non-thyroidal illness

\*\*TSH may be normal in some cases

**Question 98 of 153**

Next

A 25-year-old male develops type 2 diabetes mellitus. Which one of the following genes is most likely to be responsible?

<input type="radio"/>	A. Glucokinase
<input type="radio"/>	B. HNF-1 alpha
<input type="radio"/>	C. HNF-4 alpha
<input type="radio"/>	D. HNF-1 beta
<input type="radio"/>	E. IPF-1

Next question

**MODY**

Maturity-onset diabetes of the young (MODY) is characterised by the development of type 2 diabetes mellitus in patients < 25 years old. It is typically inherited as an autosomal dominant condition. Over six different genetic mutations have so far been identified as leading to MODY. Ketosis is not a feature at presentation

**MODY 3**

- 60% of cases
- due to a defect in the HNF-1 alpha gene

**MODY 2**

- 20% of cases
- due to a defect in the glucokinase gene

One of your patients is diagnosed with having the metabolic syndrome. Which one of the following is associated with this condition?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Endometriosis                       |
| <input type="radio"/> | B. Hypothyroidism                      |
| <input type="radio"/> | C. Asymptomatic rise in amylase levels |
| <input type="radio"/> | D. Elevated albumin levels             |
| <input type="radio"/> | E. Raised uric acid levels             |

Next question

### Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europic men and > 80cm for Europic women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure:  $> 140/90$  mmHg
- dyslipidaemia: triglycerides:  $> 1.695$  mmol/L and/or high-density lipoprotein cholesterol (HDL-C)  $< 0.9$  mmol/L (male),  $< 1.0$  mmol/L (female)
- central obesity: waist:hip ratio  $> 0.90$  (male),  $> 0.85$  (female), and/or body mass index  $> 30$  kg/m<sup>2</sup>
- microalbuminuria: urinary albumin excretion ratio  $> 20$  mg/min or albumin:creatinine ratio  $> 30$  mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome

What is the mode of inheritance of haemochromatosis?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Autosomal recessive       |
| <input type="radio"/> | B. X-linked dominant         |
| <input type="radio"/> | C. Mitochondrial inheritance |
| <input type="radio"/> | D. Autosomal dominant        |
| <input type="radio"/> | E. X-linked recessive        |

Next question

### Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6\*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

#### Epidemiology

- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

#### Presenting features

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	Irreversible complications
<ul style="list-style-type: none"> <li>• Cardiomyopathy</li> <li>• Skin pigmentation</li> </ul>	<ul style="list-style-type: none"> <li>• Liver cirrhosis**</li> <li>• Diabetes mellitus</li> <li>• Hypogonadotrophic hypogonadism</li> <li>• Arthropathy</li> </ul>

\*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

\*\*whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not



A 30-year-old woman who is investigated for obesity, hirsutism and oligomenorrhoea is diagnosed as having polycystic ovarian syndrome (PCOS) following an ultrasound scan. She is hoping to start a family and her doctor starts metformin to try and improve her fertility. What is the mechanism of action of metformin in PCOS?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Stimulates the release of insulin from the pancreas                                   |
| <input type="radio"/> | B. Blocks the insulin mediated development of multiple immature follicles in the ovaries |
| <input type="radio"/> | C. Increases peripheral insulin sensitivity  |
| <input type="radio"/> | D. Blocks the conversion of oestradiol to testosterone                                   |
| <input type="radio"/> | E. Increases hepatic gluconeogenesis   |

[Next question](#)

The majority of patients with polycystic ovarian syndrome have a degree of insulin resistance which in turn can lead to complicated changes in the hypothalamic-pituitary-ovarian axis.

### Polycystic ovarian syndrome: management

Polycystic ovarian syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. Management is complicated and problem based partly because the aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome.

#### General

- weight reduction if appropriate
- if a woman requires contraception then a combined oral contraceptive (COC) pill may help regulate her cycle and induce a monthly bleed (see below)

#### Hirsutism and acne

- a COC pill may be used help manage hirsutism. Possible options include a third generation COC which has fewer androgenic effects or co-cyprindiol which has an anti-androgen action. Both of these types of COC may carry an increased risk of venous thromboembolism
- if doesn't respond to COC then topical eflornithine may be tried
- spironolactone, flutamide and finasteride may be used under specialist supervision

#### Infertility

- weight reduction if appropriate

- the management of infertility in patients with PCOS should be supervised by a specialist. There is an ongoing debate as to whether metformin, clomifene or a combination should be used to stimulate ovulation
- a 2007 trial published in the New England Journal of Medicine suggested clomifene was the most effective treatment. There is a potential risk of multiple pregnancies with anti-oestrogen\* therapies such as clomifene. The RCOG published an opinion paper in 2008 and concluded that on current evidence metformin is

not a first line treatment of choice in the management of PCOS

- metformin is also used, either combined with clomifene or alone, particularly in patients who are obese
- gonadotrophins

\*work by occupying hypothalamic oestrogen receptors without activating them. This interferes with the binding of oestradiol and thus prevents negative feedback inhibition of FSH secretion

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Next

A 40-year-old woman complains of feeling tired all the time and putting on weight. On examination a diffuse, non-tender goitre is noted. Blood tests are ordered:

TSH	15.1 mU/l
Free T4	7.1 pmol/l
ESR	14 mm/hr
Anti-TSH receptor stimulating antibodies	Negative
Anti-thyroid peroxidase antibodies	Positive

What is the most likely diagnosis?

- ☐ A. Pituitary failure
- ☐ B. Primary atrophic hypothyroidism
- ☐ C. De Quervain's thyroiditis
- ☒ D. Hashimoto's thyroiditis
- ☐ E. Grave's disease

Next question

Hashimoto's thyroiditis = hypothyroidism + goitre + anti-TPO

This patient has Hashimoto's thyroiditis, as evidenced by the hypothyroidism, goitre and anti-thyroid peroxidase antibodies. De Quervain's thyroiditis typically causes a painful goitre and a raised ESR. Around 90% of patients with Grave's disease have anti-TSH receptor stimulating antibodies.

**Hashimoto's thyroiditis**

Hashimoto's thyroiditis is an autoimmune disorder of the thyroid gland. It is typically associated with hypothyroidism although there may be a transient thyrotoxicosis in the acute phase. It is 10 times more common in women

**Features**

- features of hypothyroidism
- goitre: firm, non-tender
- anti-thyroid peroxidase and also anti-Tg antibodies

A 24-year-old woman is found to have a blood pressure of 170/100 mmHg during a routine medical check. She is well and clinical examination is unremarkable. Blood tests show:

Na <sup>+</sup>	140 mmol/l
K <sup>+</sup>	2.6 mmol/l
Bicarbonate	31 mmol/l
Urea	3.4 mmol/l
Creatinine	77 µmol/l

Which one of the following investigations is most likely to be diagnostic?

- ☐ A. Renal ultrasound
- ☐ B. Overnight dexamethasone suppression test
- ☐ C. Renin:aldosterone ratio
- ☐ D. MR angiography
- ☐ E. 21-hydroxylase estimation

Next question

Conn's syndrome is the likely diagnosis - a renin:aldosterone ratio would be an appropriate first-line investigation. A normal clinical examination makes a diagnosis of Cushing's syndrome less likely

### Primary hyperaldosteronism

Primary hyperaldosteronism was previously thought to be most commonly caused by an adrenal adenoma, termed Conn's syndrome. However, recent studies have shown that bilateral idiopathic adrenal hyperplasia is the cause in up to 70% of cases. Differentiating between the two is important as this determines treatment. Adrenal carcinoma is an extremely rare cause of primary hyperaldosteronism

#### Features

- hypertension
- hypokalaemia (e.g. muscle weakness)
- alkalosis

#### Investigations

- high serum aldosterone
- low serum renin
- high-resolution CT abdomen

## Management

- adrenal adenoma: surgery
- bilateral adrenocortical hyperplasia: aldosterone antagonist e.g. spironolactone

\*please note that some of these notes have been copied to Wikipedia, and not vice-versa

A 49-year-old man with type 2 diabetes mellitus is reviewed. Despite weight loss and therapy with metformin and gliclazide his last HbA1c is 7.2%. Which one of the following factors would suggest that the patient may benefit from a meglitinide?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Obesity                                     |
| <input type="radio"/> | B. Not adhering to diabetic diet               |
| <input type="radio"/> | C. Problems with hypoglycaemia from gliclazide |
| <input type="radio"/> | D. Erratic lifestyle                           |
| <input type="radio"/> | E. Elderly and frail patients                  |

[Next question](#)

Meglitinides - stimulate insulin release - good for erratic lifestyle

Meglitinides stimulate insulin release and are particularly useful for post-prandial hyperglycaemia or an erratic eating schedule, as patients take them shortly before meals

### Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

#### Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

#### HbA1c

- the general target for patients is 48 mmol/mol (DCCT = 6.5%). HbA1c levels below 48 mmol/mol (DCCT = 6.5%) should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

#### Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first\*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 48 mmol/mol (DCCT = 6.5%)
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 58 mmol/mol (DCCT = 7.5%) then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% at 6 months)

#### Starting insulin

- usually commenced if HbA1c > 58 mmol/mol (DCCT = 7.5%)
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

#### Other risk factor modification

- current NICE guidelines suggest giving aspirin to all patients > 50 years and to younger patients with other significant risk factors. However, recent evidence does not support this approach. The 2010 SIGN guidelines do not advocate the use of aspirin for primary prevention in diabetics
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reached consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

\*many local protocols now recommend starting metformin upon diagnosis

Which of the following statements is true regarding the pathophysiology of diabetes mellitus?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Concordance between identical twins is higher in type 2 diabetes mellitus than type 1 |
| <input type="radio"/> | B. Patients with type 1 diabetes mellitus are rarely HLA-DR4 positive                    |
| <input type="radio"/> | C. Type 2 diabetes mellitus is associated with HLA-DR3                                   |
| <input type="radio"/> | D. Haemochromatosis is an example of primary diabetes                                    |
| <input type="radio"/> | E. Type 1 diabetes mellitus is thought to be inherited in an autosomal dominant fashion  |

Next question

Type 1 diabetes mellitus is caused by autoimmune destruction of the Beta-cells of the pancreas. Identical twins show a genetic concordance of 40%. It is associated with HLA-DR3 and DR4. It is inherited in a polygenic fashion

Type 2 diabetes mellitus is thought to be caused by a relative deficiency of insulin and the phenomenon of insulin resistance. Age, obesity and ethnicity are important aetiological factors. There is almost 100% concordance in identical twins and no HLA associations.

Haemochromatosis is an example of secondary diabetes

### Diabetes: pathophysiology

#### Type 1 DM

- autoimmune disease
- antibodies against beta cells of pancreas
- HLA DR4 > HLA DR3
- various antibodies such as islet-associated antigen (IAA) antibody and glutamic acid decarboxylase (GAD) antibody are detected in patients who later go on to develop type 1 DM - their prognostic significance is not yet clear



Which one of the following is least characteristic of Addison's disease?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Hypoglycaemia            |
| <input type="radio"/> | B. Metabolic alkalosis      |
| <input type="radio"/> | C. Hyponatraemia            |
| <input type="radio"/> | D. Hyperkalaemia            |
| <input type="radio"/> | E. Positive short ACTH test |

Next question

Addison's disease is associated with a metabolic acidosis

### Addison's disease: investigations

In a patient with suspected Addison's disease the definite investigation is a ACTH stimulation test (short Synacthen test). Plasma cortisol is measured before and 30 minutes after giving Synacthen 250ug IM. Adrenal autoantibodies such as anti-21-hydroxylase may also be demonstrated

Associated electrolyte abnormalities

- hyperkalaemia
- hyponatraemia
- hypoglycaemia
- metabolic acidosis

A 62-year-old man who had a myocardial infarction six months ago presents for review. What should his target cholesterol levels be?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Total cholesterol < 3.5 mmol/l; LDL < 1.5 mmol/l |
| <input type="radio"/> | B. Total cholesterol < 4.0 mmol/l; LDL < 2.0 mmol/l |
| <input type="radio"/> | C. Total cholesterol:HDL ratio < 5.0 mmol/l         |
| <input type="radio"/> | D. Total cholesterol:HDL ratio < 4.0 mmol/l         |
| <input type="radio"/> | E. Total cholesterol < 5.0 mmol/l; LDL < 3.0 mmol/l |

Next question

NICE adopted the JBS2 targets for secondary prevention in the 2008 guidelines

### Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

#### Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

NICE updated their lipid guidelines so that the following risk models are valid:

- Framingham
- Joint British Society 2 (JBS2)
- QRISK
- ASSIGN (Scotland only)

The 1991 Framingham equations may still be used. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- males of South Asian ethnicity - increase risk by 1.4 times

Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention

- liver function tests should be checked at baseline, within 3 months and at 12 months but not again unless clinically indicated

## **Secondary prevention**

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing simvastatin to 80mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained.

**Question 108 of 153**

Next

A 49-year-old woman is investigated for thyrotoxicosis. On examination she is noted to have a goitre containing multiple irregular nodules. Nuclear scintigraphy with technetium 99m reveals patchy uptake. What is the treatment of choice?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. Corticosteroids                    |
| <input type="radio"/> | B. Radioiodine                        |
| <input type="radio"/> | C. Block-and-replace regime           |
| <input type="radio"/> | D. Surgery                            |
| <input type="radio"/> | E. Anti-thyroid drug titration regime |

Next question

**Toxic multinodular goitre**

Toxic multinodular goitre describes a thyroid gland that contains a number of autonomously functioning thyroid nodules that secrete excess thyroid hormones

Nuclear scintigraphy reveals patchy uptake

The treatment of choice is radioiodine therapy

A 52-year-old woman with suspected diabetes mellitus has an oral glucose tolerance test, following the standard WHO protocol. The following results are obtained:

Time (hours)	Blood glucose (mmol/l)
0	5.9
2	8.4

How should these results be interpreted?

- ☐ A. Impaired fasting glucose and impaired glucose tolerance
- ☐ B. Normal
- ☐ C. Diabetes mellitus
- ☐ D. Impaired glucose tolerance
- ☐ E. Impaired fasting glucose

Next question

### Diabetes mellitus: diagnosis

The following is based on the World Health Organisation (WHO) 2006 guidelines.

#### Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

In 2011 WHO released supplementary guidance on the use of HbA1c on the diagnosis of diabetes:

- a HbA1c of greater than or equal to 6.5% (48 mmol/mol) is diagnostic of diabetes mellitus
- a HbA1c value of less than 6.5% does not exclude diabetes (i.e. it is not as sensitive as fasting samples for detecting diabetes)
- in patients without symptoms, the test must be repeated to confirm the diagnosis
- it should be remembered that misleading HbA1c results can be caused by increased red cell turnover (for example anaemia, haemoglobinopathies and pregnancy)

## **Impaired fasting glucose and impaired glucose tolerance**

A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

A 55-year-old woman with type 2 diabetes mellitus is reviewed. A decision is made to start thiazolidinedione therapy. Which one of the following points is it most relevant to consider before starting treatment?

<input type="radio"/>	A. History of oesophageal problems
<input type="radio"/>	B. Fracture risk
<input type="radio"/>	C. History of depression
<input type="radio"/>	D. History of cardiac arrhythmias
<input type="radio"/>	E. Visual acuity

[Next question](#)

There is increasing evidence thiazolidinediones increase the risk of fractures

### Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance. Rosiglitazone was withdrawn in 2010 following concerns about the cardiovascular side-effect profile.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

#### Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- bladder cancer: recent studies have showed an increased risk of bladder cancer in patients taking pioglitazone (hazard ratio 2.64)

#### NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

Which one of the following conditions may cause hypokalaemia in association with hypertension?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Gitelman syndrome              |
| <input type="radio"/> | B. 21-hydroxylase deficiency      |
| <input type="radio"/> | C. Bartter's syndrome             |
| <input type="radio"/> | D. Pheochromocytoma               |
| <input type="radio"/> | E. 11-beta hydroxylase deficiency |

Next question

21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

### Hypokalaemia and hypertension

For exams it is useful to be able to classify the causes of hypokalaemia in to those associated with hypertension, and those which are not

Hypokalaemia with hypertension

- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)
- Liddle's syndrome
- 11-beta hydroxylase deficiency\*

Carbenoxolone, an anti-ulcer drug, and liquorice excess can potentially cause hypokalaemia associated with hypertension

Hypokalaemia without hypertension

- diuretics
- GI loss (e.g. Diarrhoea, vomiting)
- renal tubular acidosis (type 1 and 2\*\*)
- Bartter's syndrome
- Gitelman syndrome

\*21-hydroxylase deficiency, which accounts for 90% of congenital adrenal hyperplasia cases, is not associated with hypertension

\*\*type 4 renal tubular acidosis is associated with hyperkalaemia



Which one of the following statements regarding NICE guidance on the primary prevention of cardiovascular disease is incorrect?

<input type="radio"/>	A. Premature coronary heart disease is defined as < 65 years in females
<input type="radio"/>	B. A 10-year risk of 15% is used to identify patients who should be considered for lipid-lowering therapy
<input type="radio"/>	C. Simvastatin 40mg on is the first line treatment in patients with a significant risk
<input type="radio"/>	D. The 1991 Framingham equations are still recommended for calculating risk
<input type="radio"/>	E. If a patient has a first degree relative with premature heart disease the risk should be multiplied by 1.5

[Next question](#)

Primary prevention CVD: 10-year risk of 20% is cut-off

## Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

### Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

NICE updated their lipid guidelines so that the following risk models are valid:

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Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

## **Secondary prevention**

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing simvastatin to 80mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained.

A 41-year-old woman presents with palpitations and heat intolerance. On examination her pulse is 90/min and a small, diffuse goitre is noted which is tender to touch. Thyroid function tests show the following:

Free T4	24 pmol/l
TSH	< 0.05 mu/l

What is the most likely diagnosis?

- ☐ A. Grave's disease
- ☐ B. Sick thyroid syndrome
- ☐ C. De Quervain's thyroiditis
- ☐ D. Hashimoto's thyroiditis
- ☐ E. Toxic multinodular goitre

Next question

Thyrotoxicosis with tender goitre = subacute (De Quervain's) thyroiditis

Whilst Grave's disease is the most common cause of thyrotoxicosis it would not cause a tender goitre. In the context of thyrotoxicosis this finding is only really seen in De Quervain's thyroiditis.

Hashimoto's thyroiditis is an autoimmune disorder of the thyroid gland. It is typically associated with hypothyroidism although there may be a transient thyrotoxicosis in the acute phase. The goitre is non-tender in Hashimoto's.

### Subacute (De Quervain's) thyroiditis

Subacute thyroiditis (also known as De Quervain's thyroiditis) is thought to occur following viral infection and typically presents with hyperthyroidism

#### Features

- hyperthyroidism
- painful goitre
- raised ESR
- globally reduced uptake on iodine-131 scan

#### Management

- usually self-limiting - most patients do not require treatment
- thyroid pain may respond to aspirin or other NSAIDs
- in more severe cases steroids are used, particularly if hypothyroidism develops

A 45-year-old woman presents with weight gain and recurrent 'dizzy' episodes. Over the past four months she has gained 20 kg. The episodes occur on an almost daily basis and are characterised by blurred vision, sweating, headaches and palpitations. Her GP checked a blood sugar during one of these episodes which was record as being 1.4 mmol/l. What is the single most useful test?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Glucagon stimulation test                                    |
| <input type="radio"/> | B. Oral glucose tolerance test with growth hormone measurements |
| <input type="radio"/> | C. Insulin + C-peptide levels during a hypoglycaemic episode    |
| <input type="radio"/> | D. Short ACTH test  |
| <input type="radio"/> | E. Insulin tolerance test                                       |

[Next question](#)

This patient has symptoms typical of an insulinoma. Whilst supervised fasting is normally the investigation of choice if this option is not given then insulin + C-peptide levels during an acute hypoglycaemic episode are useful.

## Insulinoma

An insulinoma is a neuroendocrine tumour deriving mainly from pancreatic Islets of Langerhans cells

### Basics

- most common pancreatic endocrine tumour
- 10% malignant, 10% multiple
- of patients with multiple tumours, 50% have MEN-1

### Features

- of hypoglycaemia: typically early in morning or just before meal, e.g. diplopia, weakness etc
- rapid weight gain may be seen
- high insulin, raised proinsulin:insulin ratio
- high C-peptide

### Diagnosis

- supervised, prolonged fasting (up to 72 hours)
- CT pancreas

### Management

- surgery
- diazoxide and somatostatin if patients are not candidates for surgery

You review a 70-year-old who has a long past medical history and is on multiple drugs. He has developed excessive amounts of breast tissue bilaterally. Which one of the following drugs is most likely to be responsible?

<input type="radio"/>	A. Tamoxifen
<input type="radio"/>	B. Terbinafine
<input type="radio"/>	C. Amiodarone
<input type="radio"/>	D. Goserelin (Zoladex)
<input type="radio"/>	E. Lymecline

[Next question](#)

Goserelin is a gonadorelin analogue used in the treatment of advanced prostate cancer. Tamoxifen may be used to treat gynaecomastia.

### Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

#### Causes of gynaecomastia

- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below

#### Drug causes of gynaecomastia

- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- gonadorelin analogues e.g. Goserelin, buserelin
- oestrogens, anabolic steroids

Very rare drug causes of gynaecomastia

- tricyclics
- isoniazid
- calcium channel blockers
- heroin
- busulfan
- methyldopa

An obese man presents as he is concerned about his risk of developing cardiovascular disease. Which one of the following sets of results would suggest a diagnosis of the metabolic syndrome using the Scottish Intercollegiate Guidelines Network (SIGN) criteria?

<input type="radio"/>	A. Waist circumference = 98 cm; fasting glucose = 7.2 mmol/l; HDL = 1.2 mmol/l
<input type="radio"/>	B. Triglycerides = 2.0 mmol/l; HDL = 1.2 mmol/l; fasting glucose = 5.4 mmol/l
<input type="radio"/>	C. Blood pressure = 140/90 mmHg; waist circumference = 90 cm; HDL = 1.4 mmol/l
<input type="radio"/>	D. Waist circumference = 110 cm; fasting glucose = 5.8 mmol/l; HDL = 0.8 mmol/l
<input type="radio"/>	E. LDL = 3.0 mmol/l; blood pressure = 130/80; fasting glucose = 6.4 mmol/l

[Next question](#)

Whilst all the results contain at least one factor consistent with the metabolic syndrome only option D contains three of the criteria and would hence support a diagnosis.

### Metabolic syndrome

Unfortunately there are a number of competing definitions of the metabolic syndrome around at the present time. It is thought that the key pathophysiological factor is insulin resistance.

SIGN recommend using criteria similar to those from the American Heart Association. The similarity of the International Diabetes Federation criteria should be noted. For a diagnosis of metabolic syndrome at least 3 of the following should be identified:

- elevated waist circumference: men > 102 cm, women > 88 cm
- elevated triglycerides: > 1.7 mmol/L
- reduced HDL: < 1.03 mmol/L in males and < 1.29 mmol/L in females
- raised blood pressure: > 130/85 mmHg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

The International Diabetes Federation produced a consensus set of diagnostic criteria in 2005, which are now widely in use. These require the presence of central obesity (defined as waist circumference > 94cm for Europid men and > 80cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:

- raised triglycerides level: > 1.7 mmol/L, or specific treatment for this lipid abnormality
- reduced HDL cholesterol: < 1.03 mmol/L in males and < 1.29 mmol/L in females, or specific treatment for this lipid abnormality
- raised blood pressure: > 130/85 mm Hg, or active treatment of hypertension
- raised fasting plasma glucose > 5.6 mmol/L, or previously diagnosed type 2 diabetes

In 1999 the World Health Organization produced diagnostic criteria which required the presence of diabetes mellitus, impaired glucose tolerance, impaired fasting glucose or insulin resistance, AND two of the following:

- blood pressure:  $> 140/90$  mmHg
- dyslipidaemia: triglycerides:  $> 1.695$  mmol/L and/or high-density lipoprotein cholesterol (HDL-C)  $< 0.9$  mmol/L (male),  $< 1.0$  mmol/L (female)
- central obesity: waist:hip ratio  $> 0.90$  (male),  $> 0.85$  (female), and/or body mass index  $> 30$  kg/m<sup>2</sup>
- microalbuminuria: urinary albumin excretion ratio  $> 20$  mg/min or albumin:creatinine ratio  $> 30$  mg/g

Other associated features include:

- raised uric acid levels
- non-alcoholic fatty liver disease
- polycystic ovarian syndrome



Each one of the following is associated with Pendred's syndrome, except:

<input type="radio"/>	A. Goitre
<input type="radio"/>	B. Short 4th and 5th metacarpals
<input type="radio"/>	C. Autosomal recessive inheritance
<input type="radio"/>	D. Sensorineural deafness
<input type="radio"/>	E. Euthyroid status

Next question

### Pendred's syndrome

Autosomal recessive disorder of defective iodine uptake

Features

- sensorineural deafness
- goitre
- euthyroid or mild hypothyroidism

A 62-year-old man is investigated for hypertension and proximal myopathy. On examination he is noted to have abdominal striae. Which one of the following is most associated with ectopic ACTH secretion?

- |                                  |                              |
|----------------------------------|------------------------------|
| <input type="radio"/>            | A. Carcinoid tumour          |
| <input checked="" type="radio"/> | B. Small cell lung cancer    |
| <input type="radio"/>            | C. Cardiac myxoma            |
| <input type="radio"/>            | D. Squamous cell lung cancer |
| <input type="radio"/>            | E. Adrenal carcinoma         |

[Next question](#)

Small cell lung cancer accounts 50-75% of case of ectopic ACTH

Adrenal carcinoma and cardiac myxoma are causes of ACTH independent Cushing's syndrome

### Cushing's syndrome: causes

ACTH dependent causes

- Cushing's disease (80%): pituitary tumour secreting ACTH producing adrenal hyperplasia
- ectopic ACTH production (5-10%): e.g. small cell lung cancer

ACTH independent causes

- iatrogenic: steroids
- adrenal adenoma (5-10%)
- adrenal carcinoma (rare)
- Carney complex: syndrome including cardiac myxoma
- micronodular adrenal dysplasia (very rare)

Pseudo-Cushing's

- mimics Cushing's
- often due to alcohol excess or severe depression
- causes false positive dexamethasone suppression test or 24 hr urinary free cortisol
- insulin stress test may be used to differentiate

Which one of the following combinations of treatments should be avoided in patients with type 2 diabetes mellitus?

<input type="radio"/>	A. Metformin + insulin + exenatide
<input type="radio"/>	B. Sulfonylurea + DPP-4 inhibitor
<input type="radio"/>	C. Metformin + sulfonylurea + exenatide
<input type="radio"/>	D. Metformin + DPP-4 inhibitor
<input type="radio"/>	E. Insulin + metformin + sulfonylurea

Next question

Exenatide should only be used in combination with metformin, a sulfonylurea or both.

### Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

#### Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

#### HbA1c

- the general target for patients is 48 mmol/mol (DCCT = 6.5%). HbA1c levels below 48 mmol/mol (DCCT = 6.5%) should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

#### Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies

for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first\*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains  $> 48$  mmol/mol (DCCT = 6.5%)
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c  $> 58$  mmol/mol (DCCT = 7.5%) then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI  $> 35$  kg/m<sup>2</sup>) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained ( $> 1.0$  percentage point HbA1c reduction and weight loss  $> 3\%$  at 6 months)

#### Starting insulin

- usually commenced if HbA1c  $> 58$  mmol/mol (DCCT = 7.5%)
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

#### Other risk factor modification

- current NICE guidelines suggest giving aspirin to all patients  $> 50$  years and to younger patients with other significant risk factors. However, recent evidence does not support this approach. The 2010 SIGN guidelines do not advocate the use of aspirin for primary prevention in diabetics
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM  $> 40$ -years-old were prescribed statins. Now patients  $> 40$ -years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk  $< 20\%/10$  years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reached consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is  $< 4.0$  mmol/l
- if serum triglyceride levels are  $> 4.5$  mmol/l prescribe fenofibrate

\*many local protocols now recommend starting metformin upon diagnosis

A 55-year-old accountant with type 2 diabetes mellitus comes for review. When he was diagnosed 12 months ago he was started on metformin and the dose was titrated up. His IFCC-HbA1c one year ago was 75 mmol/mol (DCCT-HbA1c 9%) and is now 69 mmol/mol (8.5%). His body mass index is 33 kg/m<sup>2</sup>. What is the most appropriate next step in management?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Add exenatide                     |
| <input type="radio"/> | B. Add sitagliptin                   |
| <input type="radio"/> | C. Add glipizide                     |
| <input type="radio"/> | D. Make no changes to his medication |
| <input type="radio"/> | E. Add pioglitazone                  |

[Next question](#)

His HbA1c is still significantly above target so some change to the medication is indicated.

The NICE type 2 diabetes mellitus guidelines would advocate the use of a sulfonylurea in this situation. This may seem slightly counterintuitive as it may increase the weight of a patient who is already obese. Why not use exenatide? However the average weight gain for a patient taking a sulfonylurea is 2 kg. It is likely the view of NICE that this modest weight gain does not offset the increased cost, need to involve secondary care and current lack of data surrounding cardiovascular endpoints of exenatide.

### Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

#### Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

#### HbA1c

- the general target for patients is 48 mmol/mol (DCCT = 6.5%). HbA1c levels below 48 mmol/mol (DCCT = 6.5%) should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

## Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first\*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 48 mmol/mol (DCCT = 6.5%)
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 58 mmol/mol (DCCT = 7.5%) then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% at 6 months)

## Starting insulin

- usually commenced if HbA1c > 58 mmol/mol (DCCT = 7.5%)
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

## Other risk factor modification

- current NICE guidelines suggest giving aspirin to all patients > 50 years and to younger patients with other significant risk factors. However, recent evidence does not support this approach. The 2010 SIGN guidelines do not advocate the use of aspirin for primary prevention in diabetics
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reached consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

\*many local protocols now recommend starting metformin upon diagnosis

Which one of the following is most likely to be found in a patient with Hashimoto's thyroiditis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Raised ESR                               |
| <input type="radio"/> | B. Anti-TSH receptor stimulating antibodies |
| <input type="radio"/> | C. Anti-thyroid peroxidase antibodies       |
| <input type="radio"/> | D. Decreased TSH                            |
| <input type="radio"/> | E. Co-existing type 2 diabetes mellitus     |

Next question

Hashimoto's thyroiditis = hypothyroidism + goitre + anti-TPO

### Hashimoto's thyroiditis

Hashimoto's thyroiditis is an autoimmune disorder of the thyroid gland. It is typically associated with hypothyroidism although there may be a transient thyrotoxicosis in the acute phase. It is 10 times more common in women

#### Features

- features of hypothyroidism
- goitre: firm, non-tender
- anti-thyroid peroxidase and also anti-Tg antibodies

Each one of the following is associated with autoimmune polyendocrinopathy syndrome type 1, except:

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Chronic mucocutaneous candidiasis             |
| <input type="radio"/> | B. Addison's disease                             |
| <input type="radio"/> | C. Primary hyperparathyroidism                   |
| <input type="radio"/> | D. Autosomal recessive inheritance               |
| <input type="radio"/> | E. A mutation of the AIRE1 gene on chromosome 21 |

Next question

### Autoimmune polyendocrinopathy syndrome

Addison's disease (autoimmune hypoadrenalism) is associated with other endocrine deficiencies in approximately 10% of patients. There are two distinct types of autoimmune polyendocrinopathy syndrome (APS), with type 2 (sometimes referred to as Schmidt's syndrome) being much more common.

APS type 2 has a polygenic inheritance and is linked to HLA DR3/DR4. Patients have Addison's disease plus either:

- type 1 diabetes mellitus
- autoimmune thyroid disease

APS type 1 is occasionally referred to as Multiple Endocrine Deficiency Autoimmune Candidiasis (MEDAC). It is a very rare autosomal recessive disorder caused by mutation of AIRE1 gene on chromosome 21

Features of APS type 1 (2 out of 3 needed)

- chronic mucocutaneous candidiasis (typically first feature as young child)
- Addison's disease
- primary hypoparathyroidism

Vitiligo can occur in both types



A 49-year-old woman with type 2 diabetes mellitus is being considered for exenatide therapy. Which one of the following is not part of the NICE criteria for starting or continuing this drug?

<input type="radio"/>	A. BMI > 35 kg/m <sup>2</sup>
<input type="radio"/>	B. Greater than 1.0 percentage point HbA1c reduction after 6 months
<input type="radio"/>	C. Has failed with insulin therapy
<input type="radio"/>	D. Has type 2 diabetes mellitus
<input type="radio"/>	E. Weight loss > 3% at 6 months

[Next question](#)

Patients do not need to have been on insulin prior to using exenatide

### Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of  $> 0.5$  percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

A 20-year-old man presents with a nine month history of weight gain. Prior to this he was of a normal weight and cannot identify any obvious lifestyle changes that would account for his obesity. On examination he is noted to have abdominal striae and a degree of proximal myopathy. Blood pressure is 130/80 mmHg. Bloods show the following:

Na <sup>+</sup>	141 mmol/l
K <sup>+</sup>	3.3 mmol/l
Bicarbonate	26 mmol/l
Urea	3.3 mmol/l
Creatinine	72 µmol/l

What is the most appropriate test to confirm the diagnosis?

- ☐ A. High-dose dexamethasone suppression test
- ☐ B. Plasma ACTH
- ☐ C. Short ACTH test
- ☐ D. 24 hour urinary free cortisol
- ☐ E. Renin:aldosterone ratio

Next question

The overnight dexamethasone suppression test is the best test to diagnosis Cushing's syndrome

There is some debate as to whether a 24 hour urinary free cortisol or an overnight dexamethasone suppression test should be used to screen patients for Cushing's. The overnight (not high-dose) dexamethasone suppression test has however been shown to be more sensitive and is now much more commonly used in clinical practice. As this is not offered then 24 hour urinary free cortisol is the next best answer

For a review comparing diagnostic methods see 'Specificity of first-line tests for the diagnosis of Cushing's syndrome: assessment in a large series, J Clin Endocrinol Metab. 2007 Nov;92(11):4123-9'

The high-dose dexamethasone suppression test is used to help differentiate the cause of Cushing's syndrome

### Cushing's syndrome: investigations

Investigations are divided into confirming Cushing's syndrome and then localising the lesion. A hypokalaemic metabolic alkalosis may be seen, along with impaired glucose tolerance. Ectopic ACTH secretion (e.g. secondary to small cell lung cancer) is characteristically associated with very low potassium levels. An insulin stress test is used to differentiate between true Cushing's and pseudo-Cushing's

### Tests to confirm Cushing's syndrome

The two most commonly used tests are:

- overnight dexamethasone suppression test (most sensitive)
- 24 hr urinary free cortisol

### **Localisation tests**

The first-line localisation is 9am and midnight plasma ACTH (and cortisol) levels. If ACTH is suppressed then a non-ACTH dependent cause is likely such as an adrenal adenoma

High-dose dexamethasone suppression test

- if pituitary source then cortisol suppressed
- if ectopic/adrenal then no change in cortisol

CRH stimulation

- if pituitary source then cortisol rises
- if ectopic/adrenal then no change in cortisol

Petrosal sinus sampling of ACTH may be needed to differentiate between pituitary and ectopic ACTH secretion

### Question 125 of 153

Which one of the following drugs used in the management of type 2 diabetes mellitus has the Medicines and Healthcare products Regulatory Agency warned is associated with an increased risk of severe pancreatitis and renal impairment?

<input type="radio"/>	A. Rosiglitazone
<input type="radio"/>	B. Metformin
<input type="radio"/>	C. Acarbose
<input checked="" type="radio"/>	D. Exenatide
<input type="radio"/>	E. Sitagliptin

[Next question](#)

### Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

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- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
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NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HbA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

Which one of the following regarding the management of thyroid problems during pregnancy is incorrect?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Maternal free thyroxine levels should be kept in the upper third of the normal reference range when treating thyrotoxicosis |
| <input type="radio"/> | B. Increased levels of thyroxine-binding globulin are seen in pregnancy  |
| <input type="radio"/> | C. Block-and-replace is preferable in pregnancy compared to antithyroid drug titration   |
| <input type="radio"/> | D. Breast feeding is safe whilst on thyroxine  |
| <input type="radio"/> | E. Untreated thyrotoxicosis increases the risk of premature labour   |

Next question

### Pregnancy: thyroid problems

In pregnancy there is an increase in the levels of thyroxine-binding globulin (TBG). This causes an increase in the levels of total thyroxine but does not affect the free thyroxine level

#### Thyrotoxicosis

Untreated thyrotoxicosis increases the risk of fetal loss, maternal heart failure and premature labour

Graves' disease is the most common cause of thyrotoxicosis in pregnancy. It is also recognised that activation of the TSH receptor by HCG may also occur - often termed transient gestational hyperthyroidism. HCG levels will fall in second and third trimester

#### Management

- propylthiouracil has traditionally been the antithyroid drug of choice. This approach was supported by the 2007 Endocrine Society consensus guidelines
- maternal free thyroxine levels should be kept in the upper third of the normal reference range to avoid fetal hypothyroidism
- thyrotrophin receptor stimulating antibodies should be checked at 30-36 weeks gestation - helps to determine risk of neonatal thyroid problems
- block-and-replace regimes should not be used in pregnancy
- radioiodine therapy is contraindicated

#### Hypothyroidism

##### Key points

- thyroxine is safe during pregnancy

- serum thyroid stimulating hormone measured in each trimester and 6-8 weeks post-partum
- some women require an increased dose of thyroxine during pregnancy
- breast feeding is safe whilst on thyroxine



A 53-year-old man with a history of type 2 diabetes mellitus is reviewed in the diabetes clinic. Twelve months ago his HbA1c was 9.7% despite maximal oral hypoglycaemic therapy. Insulin was started and his most recent HbA1c is 8.2%. He is considering applying for a HGV licence and asks for advice. What is the most appropriate advice?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. He cannot drive a heavy goods vehicle if he is taking insulin                                   |
| <input type="radio"/> | B. He may be able to apply for a HGV licence if he meets strict criteria relating to hypoglycaemia |
| <input type="radio"/> | C. He should stop insulin and start meglitinide  |
| <input type="radio"/> | D. As under 55 years of age there is no requirement to inform the DVLA                             |
| <input type="radio"/> | E. He needs to have been stable on insulin for at least 5 years before applying                    |

[Next question](#)

Patients on insulin may now hold a HGV licence if they meet strict DVLA criteria

#### DVLA: diabetes mellitus

Until recently people with diabetes who used insulin could not hold a HGV licence. The DVLA changed the rules in October 2011. The following standards need to be met (and also apply to patients using other hypoglycaemic inducing drugs such as sulfonylureas):

- there has not been any severe hypoglycaemic event in the previous 12 months
- the driver has full hypoglycaemic awareness
- the driver must show adequate control of the condition by regular blood glucose monitoring\*, at least twice daily and at times relevant to driving
- the driver must demonstrate an understanding of the risks of hypoglycaemia
- there are no other debarring complications of diabetes

From a practical point of view patients on insulin who want to apply for a Group 2 (HGV) licence need to complete a D2 form. They may also be required to produce a D4 Medical examination report.

Other specific points for group 1 drivers:

- if on insulin then patient can drive a car as long as they have hypoglycaemic awareness, not more than one episode of hypoglycaemia requiring the assistance of another person within the preceding 12 months and no relevant visual impairment. Drivers are normally contacted by DVLA

- if on tablets or exenatide no need to notify DVLA. If tablets may induce hypoglycaemia (e.g. sulfonylureas) then there must have been more than one episode of hypoglycaemia requiring the assistance of another person within the preceding 12 months
- if diet controlled alone then no requirement to inform DVLA

\*to demonstrate adequate control, the Secretary of State's Honorary Medical Advisory Panel on Diabetes Mellitus has recommended that applicants will need to have used blood glucose meters with a memory function to measure and record blood glucose levels for at least 3 months prior to submitting their application

What is the most appropriate screening investigation to exclude a phaeochromocytoma?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Ultrasound adrenals                                 |
| <input type="radio"/> | B. Phenoxybenzamine suppression test                   |
| <input type="radio"/> | C. 24 hour urinary collection of vanillylmandelic acid |
| <input type="radio"/> | D. 24 hour urinary collection of catecholamines        |
| <input type="radio"/> | E. Plasma adrenaline (morning)                         |

Next question

Phaeochromocytoma: do 24 hr urinary catecholamines, not VMA etc

A 24 hr urinary collection of catecholamines is preferred to one of vanillylmandelic acid as it has a higher sensitivity. Three 24 hour collections are needed as some patients have intermittently raised levels

### Phaeochromocytoma

Phaeochromocytoma is a rare catecholamine secreting tumour. About 10% are familial and may be associated with MEN type II, neurofibromatosis and von Hippel-Lindau syndrome

#### Basics

- bilateral in 10%
- malignant in 10%
- extra-adrenal in 10% (most common site = organ of Zuckerkandl, adjacent to the bifurcation of the aorta)

#### Tests

- 24 hr urinary collection of catecholamines

Surgery is the definitive management. The patient must first however be stabilized with medical management:

- alpha-blocker (e.g. phenoxybenzamine), given before a
- beta-blocker (e.g. propranolol)

Which one of the following types of bariatric surgery is most likely to cause significant malabsorption?

<input type="radio"/>	A. Laparoscopic-adjustable gastric banding
<input type="radio"/>	B. Roux-en-Y gastric bypass surgery
<input type="radio"/>	C. Biliopancreatic diversion with duodenal switch
<input type="radio"/>	D. Sleeve gastrectomy
<input type="radio"/>	E. Intra-gastric balloon

Next question

Biliopancreatic diversion with duodenal switch is a primarily malabsorptive procedure and reserved for patients who are very obese.

### Obesity: bariatric surgery

The use of bariatric surgery in the management of obesity has developed significantly over the past decade. It is now recognised that for many obese patients who fail to lose weight with lifestyle and drug interventions the risks and expense of long-term obesity outweigh those of surgery.

### NICE guidelines on bariatric surgery for adults

Consider surgery for people with severe obesity if:

- they have a BMI of 40 kg/m<sup>2</sup> or more, or between 35 kg/m<sup>2</sup> and 40 kg/m<sup>2</sup> and other significant disease (for example, type 2 diabetes mellitus, hypertension) that could be improved if they lost weight
- all appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- they are receiving or will receive intensive specialist management
- they are generally fit for anaesthesia and surgery
- they commit to the need for long-term follow-up

Consider surgery as a first-line option for adults with a BMI of more than 50 kg/m<sup>2</sup> in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long

Types of bariatric surgery:

- primarily restrictive: laparoscopic-adjustable gastric banding (LAGB) or sleeve gastrectomy
- primarily malabsorptive: classic biliopancreatic diversion (BPD) has now largely been replaced by biliopancreatic diversion with duodenal switch
- mixed: Roux-en-Y gastric bypass surgery

Which operation?

- LAGB produces less weight loss than malabsorptive or mixed procedures but as it has fewer complications it is normally the first-line intervention in patients with a BMI of 30-39kg/m<sup>2</sup>
- patients with a BMI > 40 kg/m<sup>2</sup> may be considered for a gastric bypass or sleeve gastrectomy. The latter may be done as a sole procedure or as an initial procedure prior to bypass
- primarily malabsorptive procedures are usually reserved for very obese patients (e.g. BMI > 60 kg/m<sup>2</sup>)

An 24-year-old woman is reviewed due to facial hirsutism. You suspect a diagnosis of polycystic ovarian syndrome (PCOS). Which one of the following features would suggest the need for further investigations before confidently making a diagnosis of PCOS?

<input type="radio"/>	A. Clitoromegaly
<input type="radio"/>	B. Acanthosis nigricans
<input type="radio"/>	C. Obesity
<input type="radio"/>	D. Amenorrhoea
<input type="radio"/>	E. Acne

[Next question](#)

Clitoromegaly is seen occasionally in PCOS but is normally associated with very high androgen levels. If clitoromegaly is found then further investigations to exclude an ovarian or adrenal androgen secreting tumour are required.

### Polycystic ovarian syndrome: features and investigation

Polycystic ovary syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. The aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome.

#### Features

- subfertility and infertility
- menstrual disturbances: oligomenorrhea and amenorrhoea
- hirsutism, acne (due to hyperandrogenism)
- obesity
- acanthosis nigricans (due to insulin resistance)

#### Investigations

- pelvic ultrasound: multiple cysts on the ovaries
- FSH, LH, prolactin, TSH, and testosterone are useful investigations: raised LH:FSH ratio is a 'classical' feature but is no longer thought to be useful in diagnosis. Prolactin may be normal or mildly elevated. Testosterone may be normal or mildly elevated - however, if markedly raised consider other causes
- check for impaired glucose tolerance

Which of the following secondary causes of hyperlipidaemia result in predominantly hypercholesterolaemia, as opposed to hypertriglyceridaemia?

<input type="radio"/>	A. Hypothyroidism
<input type="radio"/>	B. Obesity
<input type="radio"/>	C. Liver disease
<input type="radio"/>	D. Bendrofluazide
<input type="radio"/>	E. Chronic renal failure

[Next question](#)

Hypercholesterolaemia rather than hypertriglyceridaemia: nephrotic syndrome, cholestasis, hypothyroidism

### Hyperlipidaemia: secondary causes

Causes of predominantly hypertriglyceridaemia

- diabetes mellitus (types 1 and 2)
- obesity
- alcohol
- chronic renal failure
- drugs: thiazides, non-selective beta-blockers, unopposed oestrogen
- liver disease

Causes of predominantly hypercholesterolaemia

- nephrotic syndrome
- cholestasis
- hypothyroidism

A 65-year-old man known to have a carcinoid tumour of the appendix is found to have hepatic metastases. If the patient develops carcinoid syndrome, which one of the following symptoms is most likely to occur first?

<input type="radio"/>	A. Facial flushing
<input type="radio"/>	B. Headache
<input type="radio"/>	C. Vomiting
<input type="radio"/>	D. Diarrhoea
<input type="radio"/>	E. Palpitations

[Next question](#)

## Carcinoid tumours

### Carcinoid syndrome

- usually occurs when metastases are present in the liver and release serotonin into the systemic circulation
- may also occur with lung carcinoid as mediators are not 'cleared' by the liver

### Features

- flushing (often earliest symptom)
- diarrhoea
- bronchospasm
- hypotension
- right heart valvular stenosis (left heart can be affected in bronchial carcinoid)
- other molecules such as ACTH and GHRH may also be secreted resulting in, for example, Cushing's syndrome
- pellagra can rarely develop as dietary tryptophan is diverted to serotonin by the tumour

### Investigation

- urinary 5-HIAA
- plasma chromogranin A y

### Management

- somatostatin analogues e.g. octreotide
- diarrhoea: cyproheptadine may help



Which one of the following statements regarding the management of diabetes mellitus during pregnancy is incorrect?

<input type="radio"/>	A. A previous macrosomic baby is a risk factor for gestational diabetes
<input type="radio"/>	B. Diabetes complicates around 1 in 40 pregnancies
<input type="radio"/>	C. A higher dose of folic acid (5 mg/day) should be used
<input type="radio"/>	D. Metformin is contraindicated
<input type="radio"/>	E. Tight glycaemic control reduces complication rates

Next question

There is increasing evidence that metformin is safe during pregnancy

### Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies

Risk factors for gestational diabetes

- BMI of  $> 30 \text{ kg/m}^2$
- previous macrosomic baby weighing 4.5 kg or above.
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes

- if a woman has had gestational diabetes previously an oral glucose tolerance test (OGTT) should be performed at 16-18 weeks and at 28 weeks if the first test is normal
- women with any of the other risk factors should be offered an OGTT at 24-28 weeks
- currently the same WHO diagnostic criteria are used as for non-pregnant patients. There is however increasing evidence that a lower threshold should be used as treating borderline patients improves both maternal and neonatal outcomes

NICE issued guidelines on the management of diabetes mellitus in pregnancy in 2008

Management of pre-existing diabetes

- weight loss for women with BMI of  $> 27 \text{ kg/m}^2$
- stop oral hypoglycaemic agents, apart from metformin, and commence insulin
- folic acid 5 mg/day from pre-conception to 12 weeks gestation

- detailed anomaly scan at 18-20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy

#### Management of gestational diabetes

- responds to changes in diet and exercise in around 80% of women
- oral hypoglycaemic agents (metformin or glibenclamide) or insulin injections are needed if blood glucose control is poor or there is any evidence of complications (e.g. macrosomia)
- there is increasing evidence that oral hypoglycaemic agents are both safe and give similar outcomes to insulin
- hypoglycaemic medication should be stopped following delivery
- a fasting glucose should be checked at the 6 week postnatal check

Each one of the following is a cause of nephrogenic diabetes insipidus, except:

<input type="radio"/>	A. Hypocalcaemia
<input type="radio"/>	B. Sickle-cell anaemia
<input type="radio"/>	C. Lithium
<input type="radio"/>	D. Hypokalaemia
<input type="radio"/>	E. Demeclocycline

Next question

## Diabetes insipidus

Diabetes insipidus (DI) is a condition characterised by either a deficiency of antidiuretic hormone, ADH, (cranial DI) or an insensitivity to antidiuretic hormone (nephrogenic DI).

### Causes of cranial DI

- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X
- DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

### Causes of nephrogenic DI

- genetic: the more common form affects the vasopressin (ADH) receptor, the less common form results from a mutation in the gene that encodes the aquaporin 2 channel
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

### Features

- polyuria
- polydipsia

### Investigation

- high plasma osmolarity, low urine osmolarity
- water deprivation test

**Question 135 of 153**

Next

A 25-year-old man with a family history of multiple endocrine neoplasia type 1 is reviewed in clinic. What is the single most useful investigation to monitor such patients?

- ☐ A. Short synacthen test
- ☐ B. Urinary catecholamines
- ☐ C. Serum calcium
- ☐ D. Thyroid function tests
- ☐ E. Serum prolactin

[Next question](#)

The high incidence of parathyroid tumours and hypercalcaemia make serum calcium a useful indicator of MEN type 1 in suspected individuals

**Multiple endocrine neoplasia**

The table below summarises the three main types of multiple endocrine neoplasia (MEN)

MEN type I	MEN type IIa	MEN type IIb
<p>Mnemonic 'three P's':</p> <p>parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia</p> <p>pituitary (70%)</p> <p>pancreas (50%, e.g. insulinoma, gastrinoma)</p> <p>also: adrenal and thyroid</p>	<p>phaeochromocytoma</p> <p>medullary thyroid cancer (70%)</p> <p>parathyroid (60%)</p>	<p>medullary thyroid cancer</p> <p>phaeochromocytoma</p> <p>marfanoid body habitus</p> <p>neuromas</p>
<p>MEN1 gene</p> <p>Most common presentation = hypercalcaemia</p>	<p>RET oncogene</p>	<p>RET oncogene</p>

MEN is inherited as an autosomal dominant disorder

A 23-year-old woman is diagnosed with Graves' disease. Which one of the following statements regarding treatment is correct?

<input type="radio"/>	A. Block-and-replace regimes are usually of a shorter duration than carbimazole titration therapy
<input type="radio"/>	B. Concurrent administration of propranolol and carbimazole should be avoided
<input type="radio"/>	C. Patients on block-and-replace regimes have fewer side-effects than those using titration therapy
<input type="radio"/>	D. Carbimazole should be started at no higher than 10mg/day for patients commencing a titration regime
<input type="radio"/>	E. In the block-and-replace regime levothyroxine should be started at the same time as carbimazole

Next question

### Graves' disease: management

Despite many trials there is no clear guidance on the optimal management of Graves' disease. Treatment options include titration of anti-thyroid drugs (ATDs, for example carbimazole), block-and-replace regimes, radioiodine treatment and surgery. Propranolol is often given initially to block adrenergic effects

#### ATD titration

- carbimazole is started at 40mg and reduced gradually to maintain euthyroidism
- typically continued for 12-18 months
- patients following an ATD titration regime have been shown to suffer fewer side-effects than those on a block-and-replace regime

#### Block-and-replace

- carbimazole is started at 40mg
- thyroxine is added when the patient is euthyroid
- treatment typically lasts for 6-9 months

The major complication of carbimazole therapy is agranulocytosis

#### Radioiodine treatment

- contraindications include pregnancy (should be avoided for 4-6 months following treatment) and age < 16 years. Thyroid eye disease is a relative contraindication, as it may worsen the condition
- the proportion of patients who become hypothyroid depends on the dose given, but as a rule the majority of patient will require thyroxine supplementation after 5 years

A 30-year-old female is started on carbimazole 20mg bd following a diagnosis of Grave's disease. What is the best biochemical marker to assess her response to treatment?

<input type="radio"/>	A. Total T4
<input checked="" type="radio"/>	B. TSH
<input type="radio"/>	C. Free T4
<input type="radio"/>	D. ESR
<input type="radio"/>	E. Free T3

[Next question](#)

The answer the College are looking for is TSH. There is however a significant proportion of patients for whom TSH monitoring alone is insufficient. TSH may remain suppressed for several weeks as continued production of thyroid stimulating immunoglobulins seen in Grave's disease reduces the need for the pituitary to secrete TSH

### Thyrotoxicosis

Graves' disease accounts for around 50-60% of cases of thyrotoxicosis.

#### Causes

- Graves' disease
- toxic nodular goitre
- subacute (de Quervain's) thyroiditis
- post-partum thyroiditis
- acute phase of Hashimoto's thyroiditis (later results in hypothyroidism)
- toxic adenoma (Plummer's disease)
- amiodarone therapy

#### Investigation

- TSH down, T4 and T3 up
- thyroid autoantibodies
- other investigations are not routinely done but includes isotope scanning

A 54-year-old man with type 2 diabetes mellitus is reviewed in clinic. He is currently taking pioglitazone, metformin, aspirin and simvastatin. Which one of the following problems is most likely to be caused by pioglitazone?

<input type="radio"/>	A. Photosensitivity
<input type="radio"/>	B. Thrombocytopaenia
<input type="radio"/>	C. Myalgia
<input type="radio"/>	D. Peripheral oedema
<input type="radio"/>	E. Hyponatraemia

[Next question](#)

### Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance. Rosiglitazone was withdrawn in 2010 following concerns about the cardiovascular side-effect profile.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

#### Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- bladder cancer: recent studies have showed an increased risk of bladder cancer in patients taking pioglitazone (hazard ratio 2.64)

#### NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

A 52-year-old has a fasting lipid profile checked as part of an annual occupational health check. Combined with his blood pressure and current smoking status his 10-year risk of cardiovascular disease is calculated to be 23% percent. Following appropriate counselling he chooses to start simvastatin 40mg on. What should his target cholesterol be?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Total cholesterol:HDL ratio < 5                       |
| <input type="radio"/> | B. Total cholesterol < 5 mmol/l                          |
| <input type="radio"/> | C. Target cholesterol is inappropriate in this situation |
| <input type="radio"/> | D. Total cholesterol < 4 mmol/l                          |
| <input type="radio"/> | E. Total cholesterol:HDL ratio < 4                       |

[Next question](#)

In primary prevention of CVD, a target cholesterol is not appropriate

### Hyperlipidaemia: management

In 2008 NICE issued guidelines on lipid modification. Key points are summarised below.

#### Primary prevention

A systematic strategy should be used to identify people aged 40-74 who are likely to be at high risk of cardiovascular disease (CVD), defined as a 10-year risk of 20% or greater.

NICE updated their lipid guidelines so that the following risk models are valid:

- Framingham
- Joint British Society 2 (JBS2)
- QRISK
- ASSIGN (Scotland only)

The 1991 Framingham equations may still be used. It is however recommended that adjustments are made in the following situations:

- first-degree relative with a history of premature coronary heart disease (defined as < 55 years in males and < 65 years in females) - increase risk by 1.5 times if one relative affected or up to 2.0 times if more than one relative affected
- males of South Asian ethnicity - increase risk by 1.4 times



Along with lifestyle changes drug treatment should be considered for patients with a 10-year CVD risk of 20% or greater

- simvastatin 40mg on is the first line treatment
- there is no target level for total or LDL cholesterol for primary prevention
- liver function tests should be check at baseline, within 3 months and at 12 months but not again unless clinically indicated

## **Secondary prevention**

All patients with CVD should be taking a statin in the absence of any contraindication

NICE recommend increasing simvastatin to 80mg if a total cholesterol of less than 4 mmol/litre or an LDL cholesterol of less than 2 mmol/litre is not attained.

Which one of the following increases the risk of developing peripheral oedema in a patient taking pioglitazone?

<input type="radio"/>	A. Concomitant use with gliclazide
<input type="radio"/>	B. Serum sodium < 140 mmol/l
<input type="radio"/>	C. Concomitant use with insulin
<input type="radio"/>	D. Concomitant use with metformin
<input type="radio"/>	E. Serum potassium < 4.0 mmol/l

Next question

### Thiazolidinediones

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- weight gain
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- recent studies have indicated an increased risk of fractures
- bladder cancer: recent studies have showed an increased risk of bladder cancer in patients taking pioglitazone (hazard ratio 2.64)

#### NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

A 50-year-old man who is known to have obesity and hypertension comes for review. His current BMI is 38 kg/m<sup>2</sup> and blood pressure today is 154/92 mmHg despite ramipril and bendroflumethiazide. Lifestyle and a trial of orlistat have failed to reduce his weight. Which one of the following is the most suitable intervention?

<input type="radio"/>	A. Biliopancreatic diversion with duodenal switch
<input type="radio"/>	B. Laparoscopic-adjustable gastric banding
<input type="radio"/>	C. Trial of sibutramine
<input type="radio"/>	D. Referral for counselling to discuss his excessive eating
<input type="radio"/>	E. Sleeve gastrectomy

[Next question](#)

A trial of sibutramine would not be appropriate given his poorly controlled hypertension. Laparoscopic-adjustable gastric banding is the intervention of choice in patients with a BMI < 40 kg/m<sup>2</sup>.

### Obesity: bariatric surgery

The use of bariatric surgery in the management of obesity has developed significantly over the past decade. It is now recognised that for many obese patients who fail to lose weight with lifestyle and drug interventions the risks and expense of long-term obesity outweigh those of surgery.

### NICE guidelines on bariatric surgery for adults

Consider surgery for people with severe obesity if:

- they have a BMI of 40 kg/m<sup>2</sup> or more, or between 35 kg/m<sup>2</sup> and 40 kg/m<sup>2</sup> and other significant disease (for example, type 2 diabetes mellitus, hypertension) that could be improved if they lost weight
- all appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- they are receiving or will receive intensive specialist management
- they are generally fit for anaesthesia and surgery
- they commit to the need for long-term follow-up

Consider surgery as a first-line option for adults with a BMI of more than 50 kg/m<sup>2</sup> in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long

Types of bariatric surgery:

- primarily restrictive: laparoscopic-adjustable gastric banding (LAGB) or sleeve gastrectomy
- primarily malabsorptive: classic biliopancreatic diversion (BPD) has now largely been replaced by biliopancreatic diversion with duodenal switch
- mixed: Roux-en-Y gastric bypass surgery

Which operation?

- LAGB produces less weight loss than malabsorptive or mixed procedures but as it has fewer complications it is normally the first-line intervention in patients with a BMI of 30-39kg/m<sup>2</sup>
- patients with a BMI > 40 kg/m<sup>2</sup> may be considered for a gastric bypass or sleeve gastrectomy. The latter may be done as a sole procedure or as an initial procedure prior to bypass
- primarily malabsorptive procedures are usually reserved for very obese patients (e.g. BMI > 60 kg/m<sup>2</sup>)

Which one of the following statements regarding dipeptidyl peptidase-4 inhibitors in the management of type 2 diabetes mellitus is correct?

- |                                  |  |
|----------------------------------|--|
| <input type="radio"/>            | A. Metformin should always be co-prescribed                                    |
| <input checked="" type="radio"/> | B. Do not cause weight gain  |
| <input type="radio"/>            | C. Is given via a subcutaneous injection                                       |
| <input type="radio"/>            | D. An example is exenatide   |
| <input type="radio"/>            | E. Patients should be warned that hypoglycaemia is the most common side-effect |

[Next question](#)

Hypoglycaemia is rare in patients taking dipeptidyl peptidase-4 inhibitors.

### Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of  $> 0.5$  percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

A 4-year-old boy is being investigated for failure to thrive and generalised weakness. His blood pressure is normal. The following blood results are obtained:

Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	3.0 mmol/l
Urea	4.5 mmol/l
Creatinine	65 µmol/l
Bicarbonate	33 mmol/l

What is the most likely diagnosis?

- ☐ A. Conn's syndrome
- ☐ B. Bartter's syndrome
- ☐ C. Cushing's syndrome
- ☐ D. 21-hydroxylase deficiency
- ☐ E. Liddle's syndrome

Next question

Bartter's syndrome is associated with normotension

Bartter's syndrome is the most likely diagnosis. Congenital adrenal hyperplasia due to 21-hydroxylase deficiency is associated with precocious puberty rather than failure to thrive in boys. Both Conn's and Cushing's are associated with hypertension and are not common in this age group.

Liddle's syndrome is a rare autosomal dominant condition that causes hypertension and hypokalaemic alkalosis. It is thought to be caused by disordered sodium channels in the distal tubules leading to increased reabsorption of sodium.

### Bartter's syndrome

Bartter's syndrome is an inherited cause (usually autosomal recessive) of severe hypokalaemia due to defective chloride absorption at the Na<sup>+</sup> K<sup>+</sup> 2Cl<sup>-</sup> cotransporter in the ascending loop of Henle. It should be noted that it is associated with normotension (unlike other endocrine causes of hypokalaemia such as Conn's, Cushing's and Liddle's syndrome which are associated with hypertension)

Features

- usually presents in childhood, e.g. Failure to thrive
- polyuria, polydipsia
- hypokalaemia
- normotension
- weakness

A 29-year-old woman has just found out she is pregnant for the second time. Her first pregnancy was complicated by gestational diabetes. Following her first pregnancy she was told she was no longer diabetic. What is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Start insulin   |
| <input type="radio"/> | B. Start metformin and do oral glucose tolerance test at 12-14 weeks |
| <input type="radio"/> | C. Do oral glucose tolerance test at booking visit                   |
| <input type="radio"/> | D. Do oral glucose tolerance test at 16-18 weeks                     |
| <input type="radio"/> | E. Do fasting glucose at booking visit                               |

[Next question](#)

### Pregnancy: diabetes mellitus

Diabetes mellitus may be a pre-existing problem or develop during pregnancy, gestational diabetes. It complicates around 1 in 40 pregnancies

Risk factors for gestational diabetes

- BMI of  $> 30 \text{ kg/m}^2$
- previous macrosomic baby weighing 4.5 kg or above.
- previous gestational diabetes
- first-degree relative with diabetes
- family origin with a high prevalence of diabetes (South Asian, black Caribbean and Middle Eastern)

Screening for gestational diabetes

- if a woman has had gestational diabetes previously an oral glucose tolerance test (OGTT) should be performed at 16-18 weeks and at 28 weeks if the first test is normal
- women with any of the other risk factors should be offered an OGTT at 24-28 weeks
- currently the same WHO diagnostic criteria are used as for non-pregnant patients. There is however increasing evidence that a lower threshold should be used as treating borderline patients improves both maternal and neonatal outcomes

NICE issued guidelines on the management of diabetes mellitus in pregnancy in 2008

Management of pre-existing diabetes

- weight loss for women with BMI of  $> 27 \text{ kg/m}^2$
- stop oral hypoglycaemic agents, apart from metformin, and commence insulin



- folic acid 5 mg/day from pre-conception to 12 weeks gestation
- detailed anomaly scan at 18-20 weeks including four-chamber view of the heart and outflow tracts
- tight glycaemic control reduces complication rates
- treat retinopathy as can worsen during pregnancy

#### Management of gestational diabetes

- responds to changes in diet and exercise in around 80% of women
- oral hypoglycaemic agents (metformin or glibenclamide) or insulin injections are needed if blood glucose control is poor or there is any evidence of complications (e.g. macrosomia)
- there is increasing evidence that oral hypoglycaemic agents are both safe and give similar outcomes to insulin
- hypoglycaemic medication should be stopped following delivery
- a fasting glucose should be checked at the 6 week postnatal check

**Question 145 of 153**

Next

A 55-year-old female is reviewed in the diabetes clinic. The following results are obtained:

Urinalysis	protein +
HbA1c	10.0%

What average blood glucose level for the past 2 months is this most likely to represent?

<input type="radio"/>	A. 9
<input type="radio"/>	B. 10
<input type="radio"/>	C. 11
<input type="radio"/>	D. 15
<input type="radio"/>	E. There is no relation between HbA1c and average blood glucose

Next question

**Glycosylated haemoglobin**

Glycosylated haemoglobin (HbA1c) is the most widely used measure of long-term glycaemic control in diabetes mellitus. HbA1c is produced by the glycosylation of haemoglobin at a rate proportional to the glucose concentration. The level of HbA1c therefore is dependant on

- red blood cell lifespan
- average blood glucose concentration

HbA1c is generally thought to reflect the blood glucose over the previous '2-3 months' although there is some evidence it is weighed more strongly to glucose levels of the past 2-4 weeks

The relationship between HbA1c and average blood glucose is complex but has been studied by the Diabetes Control and Complications Trial (DCCT). A new internationally standardised method for reporting HbA1c has been developed by the International Federation of Clinical Chemistry (IFCC). This will report HbA1c in mmol per mol of haemoglobin without glucose attached.

HbA1c (%)	Average plasma glucose (mmol/l)	IFCC-HbA1c (mmol/mol)
5	5.5	
6	7.5	42
7	9.5	53
8	11.5	64
9	13.5	75
10	15.5	
11	17.5	
12	19.5	

From the above we can see that average plasma glucose =  $(2 * \text{HbA1c}) - 4.5$

A middle-aged man with type 2 diabetes mellitus is reviewed. Despite weight loss, metformin and gliclazide his HbA1c is 8.4%. The patient agrees to start insulin therapy. According to NICE guidelines which type of insulin should be tried initially?

<input type="radio"/>	A. Basal bolus regime
<input type="radio"/>	B. Isophane
<input type="radio"/>	C. Biphasic insulin
<input type="radio"/>	D. Glargine
<input type="radio"/>	E. Detemir

[Next question](#)

### Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

#### Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

#### HbA1c

- the general target for patients is 48 mmol/mol (DCCT = 6.5%). HbA1c levels below 48 mmol/mol (DCCT = 6.5%) should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

#### Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first\*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 48 mmol/mol (DCCT = 6.5%)
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 58 mmol/mol (DCCT = 7.5%) then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% at 6 months)

#### Starting insulin

- usually commenced if HbA1c > 58 mmol/mol (DCCT = 7.5%)
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

#### Other risk factor modification

- current NICE guidelines suggest giving aspirin to all patients > 50 years and to younger patients with other significant risk factors. However, recent evidence does not support this approach. The 2010 SIGN guidelines do not advocate the use of aspirin for primary prevention in diabetics
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reached consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

\*many local protocols now recommend starting metformin upon diagnosis

Which one of the following is least associated with gynaecomastia?

<input type="radio"/>	A. Klinefelter's syndrome
<input type="radio"/>	B. Seminoma
<input type="radio"/>	C. Liver disease
<input type="radio"/>	D. Puberty
<input type="radio"/>	E. Hypothyroidism

Next question

Gynaecomastia is seen in up to a third of men with thyrotoxicosis, but is not a feature of hypothyroidism

### Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

#### Causes of gynaecomastia

- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below

#### Drug causes of gynaecomastia

- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- gonadorelin analogues e.g. Goserelin, buserelin
- oestrogens, anabolic steroids

Very rare drug causes of gynaecomastia

- tricyclics
- isoniazid
- calcium channel blockers
- heroin
- busulfan
- methyldopa

A 54-year-old man has a routine medical for work. He is asymptomatic and clinical examination is unremarkable. Which of the following results establishes a diagnosis of impaired fasting glucose?

<input type="radio"/>	A. Fasting glucose 7.1 mmol/L on one occasion
<input type="radio"/>	B. Fasting glucose 6.8 mmol/L on two occasions
<input type="radio"/>	C. Glycosuria ++
<input type="radio"/>	D. 75g oral glucose tolerance test 2 hour value of 8.4 mmol/L
<input type="radio"/>	E. HbA1c of 6.7%

[Next question](#)

Diabetes diagnosis: fasting > 7.0, random > 11.1 - if asymptomatic need two readings

A 75g oral glucose tolerance test 2 hour value of 8.4 mmol/L would imply impaired glucose tolerance rather than impaired fasting glucose

### Diabetes mellitus: diagnosis

The following is based on the World Health Organisation (WHO) 2006 guidelines.

#### Diabetes mellitus

If the patient is symptomatic:

- fasting glucose greater than or equal to 7.0 mmol/l
- random glucose greater than or equal to 11.1 mmol/l (or after 75g oral glucose tolerance test)

If the patient is asymptomatic the above criteria apply but must be demonstrated on two separate occasions.

In 2011 WHO released supplementary guidance on the use of HbA1c on the diagnosis of diabetes:

- a HbA1c of greater than or equal to 6.5% (48 mmol/mol) is diagnostic of diabetes mellitus
- a HbA1c value of less than 6.5% does not exclude diabetes (i.e. it is not as sensitive as fasting samples for detecting diabetes)
- in patients without symptoms, the test must be repeated to confirm the diagnosis
- it should be remembered that misleading HbA1c results can be caused by increased red cell turnover (for example anaemia, haemoglobinopathies and pregnancy)

#### Impaired fasting glucose and impaired glucose tolerance



A fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)

Impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l

Diabetes UK suggests:

- 'People with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT.'

A 54-year-old obese man presents with lethargy and polyuria. A fasting blood sugar is requested:

Fasting glucose	8.4 mmol/l
-----------------	------------

He is given dietary advice and a decision is made to start metformin. What is the most appropriate prescription?

- ☐ A. Metformin 500mg od with food for 5 days then metformin 500mg bd for 5 days then metformin 500mg tds for 20 days then review
- ☐ B. Metformin 500mg tds with food
- ☐ C. Metformin 500mg od with food for 14 days then metformin 500mg bd for 14 days then review
- ☐ D. Metformin 1g tds with food
- ☐ E. Metformin 500mg tds taken at least 1 hour before meals

Next question

Metformin should be titrated slowly, leave at least 1 week before increasing dose

Gastrointestinal side-effects are more likely to occur if metformin is not slowly titrated up. The BNF advises leaving at least 1 week before increasing the dose.

### Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

#### Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

#### Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis\* with severe liver disease or renal failure

#### Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is  $> 130 \mu\text{mol/l}$  and stopping metformin if  $> 150 \mu\text{mol/l}$
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

A 56-year-old Muslim man with a history of type 2 diabetes asks for advice. He is due to start fasting for Ramadan soon and is unsure what he should do with regards to his diabetes medications. He currently takes metformin 500mg tds. What is the most appropriate advice?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Switch to subcutaneous biphasic insulin for the duration of Ramadan |
| <input type="radio"/> | B. 500 mg at the predawn meal + 1000 mg at the sunset meal             |
| <input type="radio"/> | C. No change to the metformin dose                                     |
| <input type="radio"/> | D. 1000 mg at the predawn meal + 500 mg at the sunset meal             |
| <input type="radio"/> | E. Stop metformin for the duration of Ramadan                          |

Please see the Diabetes Care link for more details.

### Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis\* with severe liver disease or renal failure

Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130  $\mu\text{mol/l}$  and stopping metformin if > 150  $\mu\text{mol/l}$
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Which one of the following features is least associated with primary hyperparathyroidism?

<input type="radio"/>	A. Depression
<input type="radio"/>	B. Polydipsia
<input type="radio"/>	C. Sensory loss
<input type="radio"/>	D. Peptic ulceration
<input type="radio"/>	E. Hypertension

Next question

### Primary hyperparathyroidism

In exams primary hyperparathyroidism is stereotypically seen in elderly females with an unquenchable thirst and an inappropriately normal or raised parathyroid hormone level. It is most commonly due to a solitary adenoma

Causes of primary hyperparathyroidism

- 80%: solitary adenoma
- 15%: hyperplasia
- 4%: multiple adenoma
- 1%: carcinoma

Features - 'bones, stones, abdominal groans and psychic moans'

- polydipsia, polyuria
- peptic ulceration/constipation/pancreatitis
- bone pain/fracture
- renal stones
- depression
- hypertension

Associations

- hypertension
- multiple endocrine neoplasia: MEN I and II

Investigations

- raised calcium, low phosphate

- PTH may be raised or normal
- technetium-MIBI subtraction scan

## Treatment

- total parathyroidectomy

A 51-year-old woman is reviewed in the diabetes clinic. She was diagnosed with type 2 diabetes mellitus 12 months ago and still has poor glycaemic control. She has recently had to stop taking gliclazide due to repeated episodes of hypoglycaemia and is only taking maximum dose metformin. Her BMI is 26 kg/m<sup>2</sup>. What is the most appropriate next step in management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Add either a thiazolidinedione or a DPP-4 inhibitor |
| <input type="radio"/> | B. Refer her for a laparoscopic gastric band           |
| <input type="radio"/> | C. Refer her for insulin therapy                       |
| <input type="radio"/> | D. Add either a thiazolidinedione or exenatide         |
| <input type="radio"/> | E. Add either a DPP-4 inhibitor or exenatide           |

[Next question](#)

### Diabetes mellitus: management of type 2

NICE updated its guidance on the management of type 2 diabetes mellitus (T2DM) in 2009. Key points are listed below:

#### Dietary advice

- encourage high fibre, low glycaemic index sources of carbohydrates
- include low-fat dairy products and oily fish
- control the intake of foods containing saturated fats and trans fatty acids
- limited substitution of sucrose-containing foods for other carbohydrates is allowable, but care should be taken to avoid excess energy intake
- discourage use of foods marketed specifically at people with diabetes
- initial target weight loss in an overweight person is 5-10%

#### HbA1c

- the general target for patients is 48 mmol/mol (DCCT = 6.5%). HbA1c levels below 48 mmol/mol (DCCT = 6.5%) should not be pursued
- however, individual targets should be agreed with patients to encourage motivation
- HbA1c should be checked every 2-6 months until stable, then 6 monthly

#### Blood pressure

- target is < 140/80 mmHg (or < 130/80 mmHg if end-organ damage is present)
- ACE inhibitors are first-line

The NICE treatment algorithm has become much more complicated following the introduction of new therapies for type 2 diabetes. We suggest reviewing this using the link provided. Below is a very selected group of points from the algorithm:

- NICE still suggest a trial of lifestyle interventions first\*
- usually metformin is first-line, followed by a sulfonylurea if the HbA1c remains > 48 mmol/mol (DCCT = 6.5%)
- if the patient is at risk from hypoglycaemia (or the consequences of) then a DPP-4 inhibitor or thiazolidinedione should be considered rather than a sulfonylurea
- meglitinides (insulin secretagogues) should be considered for patients with an erratic lifestyle
- if HbA1c > 58 mmol/mol (DCCT = 7.5%) then consider human insulin
- metformin treatment should be continued after starting insulin
- exenatide should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely. Continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% at 6 months)

#### Starting insulin

- usually commenced if HbA1c > 58 mmol/mol (DCCT = 7.5%)
- NICE recommend starting with human NPH insulin (isophane, intermediate acting) taken at bed-time or twice daily according to need

#### Other risk factor modification

- current NICE guidelines suggest giving aspirin to all patients > 50 years and to younger patients with other significant risk factors. However, recent evidence does not support this approach. The 2010 SIGN guidelines do not advocate the use of aspirin for primary prevention in diabetics
- the management of blood lipids in T2DM has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information.
- if serum cholesterol target not reached consider increasing simvastatin to 80mg on
- if target still not reached consider using a more effective statin (e.g. Atorvastatin) or adding ezetimibe
- target total cholesterol is < 4.0 mmol/l
- if serum triglyceride levels are > 4.5 mmol/l prescribe fenofibrate

\*many local protocols now recommend starting metformin upon diagnosis



### Question 153 of 153

A 62-year-old male with a history of type 2 diabetes mellitus is investigated for lethargy. Blood tests are as follows:

Na <sup>+</sup>	139 mmol/l
K <sup>+</sup>	4.2 mmol/l
Bicarbonate	15 mmol/l
Chloride	105 mmol/l
Urea	15.2 mmol/l
Creatinine	267 µmol/l
Glucose	9.2 mmol/l

Which one of the following is most likely to be contributing to the low bicarbonate value?

- ☐ A. Vomiting due to gastroparesis
- ☐ B. Renal tubular acidosis
- ☐ C. Addison's disease
- ☐ D. Metformin
- ☐ E. Rosiglitazone

Whilst the decreased bicarbonate value may be worsened by deteriorating renal function, it is important to exclude lactic acidosis secondary to metformin.

The raised anion gap is against a diagnosis of renal tubular acidosis.

#### Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

#### Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

#### Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%

- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis\* with severe liver disease or renal failure

#### Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is  $> 130 \mu\text{mol/l}$  and stopping metformin if  $> 150 \mu\text{mol/l}$
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

**Question 1 of 139**

Next

A 30-year-old man is investigated for enlarged, painless cervical lymph nodes. A biopsy is taken and a diagnosis of Hodgkin's lymphoma is made. Which one of the following types of Hodgkin's lymphoma carries the best prognosis?

<input type="radio"/>	A. Lymphocyte predominant
<input type="radio"/>	B. Mixed cellularity
<input type="radio"/>	C. Nodular sclerosing
<input type="radio"/>	D. Hairy cell
<input type="radio"/>	E. Lymphocyte depleted

Next question

Hodgkin's lymphoma - best prognosis = lymphocyte predominant

**Hodgkin's lymphoma: histological classification and prognosis**

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

**Histological classification**

- nodular sclerosing: most common, good prognosis
- mixed cellularity: good prognosis
- lymphocyte predominant: best prognosis
- lymphocyte depleted: least common, worst prognosis

'B' symptoms also imply a poor prognosis

- weight loss > 10% in last 6 months
- fever > 38°C
- night sweats

Other factors associated with a poor prognosis identified in a 1998 NEJM paper included:

- age > 45 years
- stage IV disease
- haemoglobin < 10.5 g/dl
- lymphocyte count < 600/ $\mu$ l or < 8%
- male
- albumin < 40 g/l
- white blood count > 15,000/ $\mu$ l

**Question 2 of 139**

Next

Which one of the following cytotoxic agents acts by inhibiting dihydrofolate reductase and thymidylate synthesis?

- ☐ A. Methotrexate
- ☐ B. Vincristine
- ☐ C. Bleomycin
- ☐ D. Cyclophosphamide
- ☐ E. Doxorubicin

Next question

**Cytotoxic agents**

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

**Question 3 of 139**

Next

A 4-year-old boy is admitted after developing a haemarthrosis in his right knee whilst playing in the garden. The following blood results are obtained:

Platelets	220 * 10 <sup>9</sup> /l
PT	11 secs
APTT	76 secs
Factor VIIIc activity	Normal

What is the most likely diagnosis?

- ☐ A. Antithrombin III deficiency
- ☐ B. Von Willebrand's disease
- ☐ C. Antiphospholipid syndrome
- ☐ D. Haemophilia A
- ☐ E. Haemophilia B

Next question

A grossly elevated APTT may be caused by heparin therapy, haemophilia or antiphospholipid syndrome. A normal factor VIIIc activity points to a diagnosis of haemophilia B (lack of factor IX). Antiphospholipid syndrome is a prothrombotic condition

**Haemophilia**

Haemophilia is a X-linked recessive disorder of coagulation. Up to 30% of patients have no family history of the condition. Haemophilia A is due to a deficiency of factor VIII whilst in haemophilia B (Christmas disease) there is a lack of factor IX

**Features**

- haemarthroses, haematomas
- prolonged bleeding after surgery or trauma

**Blood tests**

- prolonged APTT
- bleeding time, thrombin time, prothrombin time normal

Up to 10-15% of patients with haemophilia A develop antibodies to factor VIII treatment

**Question 4 of 139**

Next

A 45-year-old woman is diagnosed with non-Hodgkin's lymphoma. She is a recovering alcoholic and has been left with significant alcohol-related peripheral neuropathy. Which one of the following chemotherapy agents should be avoided if possible, given her past history?

- ☐ A. Doxorubicin
- ☐ B. Vincristine
- ☐ C. Chlorambucil
- ☐ D. Docetaxel
- ☐ E. Cyclophosphamide

Vincristine - peripheral neuropathy

**Cytotoxic agents**

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

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Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis
---------------------	---	---

Next

### Question 5 of 139

A 56-year-old man with metastatic prostate cancer comes for review. He is known to have spinal metastases but until now has not had any significant problems with pain control. Unfortunately he is now getting regular back pain despite taking paracetamol 1g qds. Neurological examination is unremarkable. What is the most appropriate next step?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. Switch to co-codamol 30/500 |
| <input type="radio"/> | B. Refer for radiotherapy      |
| <input type="radio"/> | C. Add oral bisphosphonate     |
| <input type="radio"/> | D. Add diclofenac              |
| <input type="radio"/> | E. Add dexamethasone           |

Next question

Metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

Bone pain often responds well to NSAIDs. Both radiotherapy and bisphosphonates have a role in managing bony pain but these are not first-line treatments

### Palliative care prescribing: pain

#### NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

#### Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered

#### SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points



- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

### Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

### Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

### Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted. NICE give the following advice on conversion:

- a transdermal fentanyl 12 microgram patch equates to approximately 45 mg oral morphine daily
- a transdermal buprenorphine 20 microgram patch equates to approximately 30 mg oral morphine daily.

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

### Question 6 of 139

A 50-year-old man with a history of ulcerative colitis comes for review. Six years ago he had an ileostomy formed which has been functioning well until now. Unfortunately he is currently suffering significant pain around the stoma site. On examination a deep erythematous ulcer is noted with a ragged edge. The surrounding skin is erythematous and swollen. What is the most likely diagnosis?

<input type="radio"/>	A. Munchausen's syndrome
<input type="radio"/>	B. Irritant contact dermatitis
<input type="radio"/>	C. Pyoderma gangrenosum
<input type="radio"/>	D. Dermatitis artefacta
<input type="radio"/>	E. Stomal granuloma

[Next question](#)

Pyoderma gangrenosum is associated with inflammatory bowel disease and may be seen around the stoma site. Treatment is usually with immunosuppressants as surgery may worsen the problem

A differential diagnosis would be malignancy and hence lesions should be referred for specialist opinion to evaluate the need for a biopsy. Irritant contact dermatitis is common but would not be expected to cause such a deep ulcer.

### Pyoderma gangrenosum

#### Features

- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

#### Causes\*

- idiopathic in 50%
- inflammatory bowel disease: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

#### Management

- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

\*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

Which one of the following is least likely to cause a warm autoimmune haemolytic anaemia?

<input type="radio"/>	A. Mycoplasma infection
<input type="radio"/>	B. Methyldopa
<input type="radio"/>	C. Chronic lymphocytic leukaemia
<input type="radio"/>	D. Lymphoma
<input type="radio"/>	E. Systemic lupus erythematosus

Mycoplasma infection causes a cold autoimmune haemolytic anaemia. Systemic lupus erythematosus can rarely be associated with a mixed-type autoimmune haemolytic anaemia

### Autoimmune haemolytic anaemia

Autoimmune haemolytic anaemia (AIHA) may be divided into 'warm' and 'cold' types, according to at what temperature the antibodies best cause haemolysis. It is most commonly idiopathic but may be secondary to a lymphoproliferative disorder, infection or drugs. AIHA is characterised by a positive direct antiglobulin test (Coombs' test)

#### Warm AIHA

In warm AIHA the antibody (usually IgG) causes haemolysis best at body temperature and haemolysis tends to occur in extravascular sites, for example the spleen. Management options include steroids, immunosuppression and splenectomy

Causes of warm AIHA

- autoimmune disease: e.g. systemic lupus erythematosus\*
- neoplasia: e.g. lymphoma, CLL
- drugs: e.g. methyldopa

#### Cold AIHA

The antibody in cold AIHA is usually IgM and causes haemolysis best at 4 deg C. Haemolysis is mediated by complement and is more commonly intravascular. Features may include symptoms of Raynaud's and acrocyanosis. Patients respond less well to steroids

Causes of cold AIHA

- neoplasia: e.g. lymphoma
- infections: e.g. mycoplasma, EBV

\*systemic lupus erythematosus can rarely be associated with a mixed-type autoimmune haemolytic anaemia

A 33-year-old male patient with a history of recurrent nose bleeds, iron-deficiency anaemia and dyspnoea is found to have a pulmonary AV malformation on pulmonary angiography. What is the likely underlying diagnosis?

<input type="radio"/>	A. Haemophilia A
<input checked="" type="radio"/>	B. Hereditary haemorrhagic telangiectasia
<input type="radio"/>	C. Mantle cell lymphoma
<input type="radio"/>	D. Wegener's granulomatosis
<input type="radio"/>	E. Down's syndrome

[Next question](#)

### Hereditary haemorrhagic telangiectasia

Also known as Osler-Weber-Rendu syndrome, hereditary haemorrhagic telangiectasia (HHT) is an autosomal dominant condition characterised by (as the name suggests) multiple telangiectasia over the skin and mucous membranes. Twenty percent of cases occur spontaneously without prior family history.

There are 4 main diagnostic criteria. If the patient has 2 then they are said to have a possible diagnosis of HHT. If they meet 3 or more of the criteria they are said to have a definite diagnosis of HHT:

- epistaxis : spontaneous, recurrent nosebleeds
- telangiectases: multiple at characteristic sites (lips, oral cavity, fingers, nose)
- visceral lesions: for example gastrointestinal telangiectasia (with or without bleeding), pulmonary arteriovenous malformations (AVM), hepatic AVM, cerebral AVM, spinal AVM
- family history: a first-degree relative with HHT

A blood film is reported as follows:

Howell-Jolly bodies, target cells and occasional Pappenheimer bodies are seen

What is the most likely underlying cause?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Iron-deficiency anaemia |
| <input type="radio"/> | B. Lead poisoning          |
| <input type="radio"/> | C. Myelofibrosis           |
| <input type="radio"/> | D. Sideroblastic anaemia   |
| <input type="radio"/> | E. Post-splenectomy        |

### Blood films: typical pictures

Hyposplenism e.g. post-splenectomy

- target cells
- Howell-Jolly bodies
- Pappenheimer bodies
- siderotic granules
- acanthocytes
- schizocytes

Iron-deficiency anaemia

- target cells
- 'pencil' poikilocytes
- if combined with B12/folate deficiency a 'dimorphic' film occurs with mixed microcytic and macrocytic cells

Myelofibrosis

- 'tear-drop' poikilocytes

Intravascular haemolysis

- schistocytes

Megaloblastic anaemia

- hypersegmented neutrophils

A 22-year-old man with sickle cell anaemia presents with pallor, lethargy and a headache. Blood results are as follows:

Hb	4.6 g/dl
Reticulocytes	3%

Infection with a parvovirus is suspected. What is the likely diagnosis?

- ☐ A. Thrombotic crisis
- ☐ B. Sequestration crisis
- ☐ C. Transformation to myelodysplasia
- ☐ D. Haemolytic crisis
- ☐ E. Aplastic crisis

Next question

The sudden fall in haemoglobin without an appropriate reticulocytosis (3% is just above the normal range) is typical of an aplastic crisis, usually secondary to parvovirus infection

### Sickle-cell crises

Sickle cell anaemia is characterised by periods of good health with intervening crises

Four main types of crises are recognised:

- thrombotic, 'painful crises'
- sequestration
- aplastic
- haemolytic

#### Thrombotic crises

- also known as painful crises or vaso-occlusive crises
- precipitated by infection, dehydration, deoxygenation
- infarcts occur in various organs including the bones (e.g. avascular necrosis of hip, hand-foot syndrome in children, lungs, spleen and brain)

#### Sequestration crises

- sickling within organs such as the spleen or lungs causes pooling of blood with worsening of the anaemia
- acute chest syndrome: dyspnoea, chest pain, pulmonary infiltrates, low pO<sub>2</sub> - the most common cause of death after childhood

### Aplastic crises

- caused by infection with parvovirus
- sudden fall in haemoglobin

### Haemolytic crises

- rare
- fall in haemoglobin due an increased rate of haemolysis



Which one of the following factors is most associated with an increased risk of developing bladder cancer?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Strongyloides stercoralis infection |
| <input type="radio"/> | B. Beryllium salt exposure             |
| <input type="radio"/> | C. Aniline dye exposure                |
| <input type="radio"/> | D. Aflatoxin exposure                  |
| <input type="radio"/> | E. Long term phenytoin use             |

Next question

### Bladder cancer: risk factors

The following factors are associated with the development of bladder cancer:

- smoking
- occupational: aniline dyes used in printing and textile industry, rubber manufacture
- schistosomiasis
- drugs: cyclophosphamide

Which one of the following is not a feature of paroxysmal nocturnal haemoglobinuria?

<input type="radio"/>	A. Haemolytic anaemia
<input type="radio"/>	B. Positive Ham test
<input type="radio"/>	C. Haemoglobinuria
<input type="radio"/>	D. Aplastic anaemia
<input type="radio"/>	E. Haemarthrosis

Next question

### Paroxysmal nocturnal haemoglobinuria

Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired disorder leading to haemolysis (mainly intravascular) of haematological cells. It is thought to be caused by increased sensitivity of cell membranes to complement (see below) due to a lack of glycoprotein glycosyl-phosphatidylinositol (GPI). Patients are more prone to venous thrombosis

#### Pathophysiology

- GPI can be thought of as an anchor which attaches surface proteins to the cell membrane
- complement-regulating surface proteins, e.g. decay-accelerating factor (DAF), are not properly bound to the cell membrane due a lack of GPI
- thrombosis is thought to be caused by a lack of CD59 on platelet membranes predisposing to platelet aggregation

#### Features

- haemolytic anaemia
- red blood cells, white blood cells, platelets or stem cells may be affected therefore pancytopenia may be present
- haemoglobinuria: classically dark-coloured urine in the morning (although has been shown to occur throughout the day)
- thrombosis e.g. Budd-Chiari syndrome
- aplastic anaemia may develop in some patients

#### Diagnosis

- flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in PNH
- Ham's test: acid-induced haemolysis (normal red cells would not)

## Management

- blood product replacement
- anticoagulation
- eculizumab, a monoclonal antibody directed against terminal protein C5, is currently being trialled and is showing promise in reducing intravascular haemolysis
- stem cell transplantation

**Question 13 of 139**

Next

A 21-year-old man comes for review. He recently had an abdominal ultrasound for episodic right upper quadrant pain which demonstrated gallstones. A full blood count was also ordered which was reported as follows:

Hb	9.8 g/dl
MCV	91 fl
Plt	$177 \times 10^9/l$
WBC	$5.3 \times 10^9/l$

The patient also mentions that his father had a splenectomy at the age of 30 years. Which one of the following tests is most likely to be diagnostic?

- ☐ A. Ham's test
- ☐ B. PAS staining of erythrocytes
- ☐ C. Glucose-6-phosphate dehydrogenase levels
- ☐ D. Osmotic fragility test
- ☐ E. Direct Coombs' test

Next question

This patient has hereditary spherocytosis as evidenced by the normocytic anaemia, gallstones and family history.

**Hereditary spherocytosis****Basics**

- most common hereditary haemolytic anaemia in people of northern European descent
- autosomal dominant defect of red blood cell cytoskeleton
- the normal biconcave disc shape is replaced by a sphere-shaped red blood cell
- red blood cell survival reduced as destroyed by the spleen

**Presentation**

- failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable

**Diagnosis**

- osmotic fragility test

## Management

- folate replacement
- splenectomy

**Question 14 of 139**

Next

A 42-year-old female is noted to have a Hb of 17.8 g/dL. Which one of the following is least likely to be the cause?

<input type="radio"/>	A. Polycythaemia rubra vera
<input type="radio"/>	B. Chronic obstructive pulmonary disease
<input type="radio"/>	C. Hypernephroma
<input type="radio"/>	D. Haemochromatosis
<input type="radio"/>	E. Dehydration

Next question

Haemochromatosis is not associated with polycythaemia. Blood tests typically reveal a raised ferritin and iron, associated with a transferrin saturation of greater than 60% and a low total iron binding capacity

**Polycythaemia**

Polycythaemia may be relative, primary (polycythaemia rubra vera) or secondary

Relative causes

- dehydration
- stress: Gaisbock syndrome

Primary

- polycythaemia rubra vera

Secondary causes

- COPD
- altitude
- obstructive sleep apnoea
- excessive erythropoietin: cerebellar haemangioma, hypernephroma, hepatoma, uterine fibroids\*

To differentiate between true (primary or secondary) polycythaemia and relative polycythaemia red cell mass studies are sometimes used. In true polycythaemia the total red cell mass in males > 35 ml/kg and in women > 32 ml/kg

\*uterine fibroids may cause menorrhagia which in turn leads to blood loss - polycythaemia is rarely a clinical problem

**Question 15 of 139**

Next

Which one of the following is a marker of a bad prognosis in acute lymphoblastic leukaemia?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Pre-B phenotype                                |
| <input type="radio"/> | B. Presentation in childhood                      |
| <input type="radio"/> | C. Initial white cell count of $18 \times 10^9/l$ |
| <input type="radio"/> | D. Female sex                                     |
| <input type="radio"/> | E. Philadelphia chromosome positive               |

Next question

Philadelphia translocation, t(9;22) - good prognosis in CML, poor prognosis in AML + ALL

**Acute lymphoblastic leukaemia: prognostic features**

Good prognostic factors

- French-American-British (FAB) L1 type
- common ALL
- pre-B phenotype
- low initial WBC

Poor prognostic factors

- FAB L3 type
- T or B cell surface markers
- Philadelphia translocation, t(9;22)
- age < 2 years or > 10 years
- male sex
- CNS involvement
- high initial WBC (e.g.  $> 100 \times 10^9/l$ )
- non-Caucasian

A 34-year-old man who is HIV positive is starting treatment for Burkitt's lymphoma. His chemotherapy regime includes cyclophosphamide, vincristine, methotrexate and prednisolone. Around 24 hours after starting chemotherapy he becomes confused and complains of muscle cramps in his legs. Which one of the following is most likely to have occurred?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Prednisolone-induced psychosis                       |
| <input type="radio"/> | B. Hypercalcaemia                                       |
| <input type="radio"/> | C. Methotrexate pneumonitis leading to hypoxia          |
| <input type="radio"/> | D. Haemorrhagic cystitis leading to acute renal failure |
| <input type="radio"/> | E. Tumour lysis syndrome                                |

[Next question](#)

Burkitt's lymphoma is a common cause of tumour lysis syndrome

Tumour lysis syndrome occurs as a result of cell breakdown following chemotherapy. This releases a large quantity of intracellular components such as potassium, phosphate and uric acid.

### Burkitt's lymphoma

Burkitt's lymphoma is a high-grade B-cell neoplasm. There are two major forms:

- endemic (African) form: typically involves maxilla or mandible
- sporadic form: abdominal (e.g. ileo-caecal) tumours are the most common form. More common in patients with HIV

Burkitt's lymphoma is associated with the c-myc gene translocation, usually t(8:14). The Epstein-Barr virus (EBV) is strongly implicated in the development of the African form of Burkitt's lymphoma and to a lesser extent the sporadic form.

Management is with chemotherapy. This tends to produce a rapid response which may cause 'tumour lysis syndrome'. Complications of tumour lysis syndrome include:

- hyperkalaemia
- hyperphosphataemia
- hypocalcaemia
- hyperuricaemia
- acute renal failure



Which one of the following may be used to monitor patients with colorectal cancer?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. CA-125                   |
| <input type="radio"/> | B. Carcinoembryonic antigen |
| <input type="radio"/> | C. Alpha-fetoprotein        |
| <input type="radio"/> | D. CA 19-9                  |
| <input type="radio"/> | E. CA 15-3                  |

Next question

Carcinoembryonic antigen may be used to monitor for recurrence in patients post-operatively or to assess response to treatment in patients with metastatic disease

### Colorectal cancer: screening

#### Overview

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screening programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligible patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cancer

A 66-year-old woman with a history of chronic kidney disease stage 4 metastatic breast cancer is admitted with a swollen right calf. Investigations confirm a deep vein thrombosis and she is started on treatment dose dalteparin. As she has a significant degree of renal impairment it is decided to monitor her response to dalteparin. What is the most appropriate blood test to perform?

- ☐ A. Anti-Factor Xa levels
- ☐ B. Antithrombin III levels
- ☐ C. Anti-Factor VIIIa levels
- ☐ D. Protrombin time (PT)
- ☐ E. Activated Partial Thromboplastin Time (APTT)

[Next question](#)

## Heparin

There are two main types of heparin - unfractionated, 'standard' heparin or low molecular weight heparin (LMWH). Heparins generally act by activating antithrombin III. Unfractionated heparin forms a complex which inhibits thrombin, factors Xa, IXa, XIa and XIIa. LMWH however only increases the action of antithrombin III on factor Xa

The table below shows the differences between standard heparin and LMWH:

	Standard heparin	Low molecular weight heparin (LMWH)
<b>Administration</b>	Intravenous	Subcutaneous
<b>Duration of action</b>	Short	Long
<b>Mechanism of action</b>	Activates antithrombin III. Forms a complex that inhibits thrombin, factors Xa, IXa, XIa and XIIa	Activates antithrombin III. Forms a complex that inhibits factor Xa
<b>Side-effects</b>	Bleeding Heparin-induced thrombocytopenia (HIT) Osteoporosis	Bleeding  Lower risk of HIT and osteoporosis with LMWH
<b>Monitoring</b>	Activated partial thromboplastin time (APTT)	Anti-Factor Xa (although routine monitoring is not required)
<b>Notes</b>	Useful in situations where there is a high risk of bleeding as anticoagulation can be terminated	Now standard in the management of venous thromboembolism treatment and prophylaxis and acute

	rapidly	coronary syndromes
--	---------	--------------------

#### Heparin-induced thrombocytopenia (HIT)

- immune mediated - antibodies form which cause the activation of platelets
- usually does not develop until after 5-10 days of treatment
- despite being associated with low platelets HIT is actually a prothrombotic condition
- features include a greater than 50% reduction in platelets, thrombosis and skin allergy
- treatment options include alternative anticoagulants such as lepirudin and danaparoid

Both unfractionated and low-molecular weight heparin can cause hyperkalaemia. This is thought to be caused by inhibition of aldosterone secretion.

Heparin overdose may be reversed by protamine sulphate, although this only partially reverses the effect of LMWH.

A 52-year-old man with a history of anaemia and abdominal discomfort is diagnosed as having chronic myeloid leukaemia. What is the mechanism of action of imatinib?

- |                                  |                                  |
|----------------------------------|----------------------------------|
| <input type="radio"/>            | A. EGF receptor antagonist       |
| <input checked="" type="radio"/> | B. Tyrosine kinase inhibitor     |
| <input type="radio"/>            | C. Anti-CD52 monoclonal antibody |
| <input type="radio"/>            | D. Anti-CD23 monoclonal antibody |
| <input type="radio"/>            | E. p53 inhibitor                 |

[Next question](#)

Chronic myeloid leukaemia - imatinib = tyrosine kinase inhibitor

Imatinib is an inhibitor of the tyrosine kinase associated with the BCR-ABL defect

### Chronic myeloid leukaemia

The Philadelphia chromosome is present in more than 95% of patients with chronic myeloid leukaemia (CML). It is due to a translocation between the long arm of chromosome 9 and 22 - t(9:22)(q34; q11). This results in part of the ABL proto-oncogene from chromosome 9 being fused with the BCR gene from chromosome 22. The resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal

Presentation (40-50 years)

- middle-age
- anaemia, weight loss, abdo discomfort
- splenomegaly may be marked
- spectrum of myeloid cells seen in peripheral blood
- decreased neutrophil alkaline phosphatase
- may undergo blast transformation (AML in 80%, ALL in 20%)

### Management

- imatinib is now considered first-line treatment
- hydroxyurea
- interferon-alpha
- allogenic bone marrow transplant

### Imatinib

- inhibitor of the tyrosine kinase associated with the BCR-ABL defect
- very high response rate in chronic phase CML

**Question 20 of 139**

Next

A 67-year-old man with a 10-year history of gastro-oesophageal reflux disease is investigated for dysphagia. An endoscopy shows an obstructive lesion highly suspicious of oesophageal cancer. What is the biopsy most likely to show?

<input type="radio"/>	A. Squamous cell carcinoma
<input type="radio"/>	B. Normal squamous epithelium
<input type="radio"/>	C. Adenocarcinoma
<input type="radio"/>	D. Leiomyoma
<input type="radio"/>	E. Metaplastic columnar epithelium

Next question

Oesophageal adenocarcinoma is associated with GORD or Barrett's

Metaplastic columnar epithelium would be seen with Barrett's but this is not consistent with the obstructive lesion seen on endoscopy.

**Oesophageal cancer**

Until recent times oesophageal cancer was most commonly due to a squamous cell carcinoma but the incidence of adenocarcinoma is rising rapidly. Adenocarcinoma is now the most common type of oesophageal cancer and is more likely to develop in patients with a history of gastro-oesophageal reflux disease (GORD) or Barrett's.

The majority of tumours are in the middle third of the oesophagus.

**Risk factors**

- smoking
- alcohol
- GORD
- Barrett's oesophagus
- achalasia
- Plummer-Vinson syndrome
- rare: coeliac disease, scleroderma

**Question 21 of 139**

Next

A 72-year-old woman is found to have a marked lymphocytosis associated with smudge cells on the blood film. A diagnosis of chronic lymphocytic leukaemia is suspected. Which one of the following is the investigation of choice?

<input type="radio"/>	A. Immunophenotyping
<input type="radio"/>	B. Bone marrow aspiration
<input type="radio"/>	C. Protein electrophoresis
<input type="radio"/>	D. White cell scan
<input type="radio"/>	E. Bone marrow trephine

Next question

CLL - immunophenotyping is investigation of choice

Immunophenotyping will demonstrate the cells to be B-cells (CD19 positive). CD5 and CD23 are also characteristically positive in chronic lymphocytic leukaemia

**Chronic lymphocytic leukaemia**

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

**Features**

- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

**Complications**

- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

**Investigations**

- blood film: smudge cells
- immunophenotyping

**Question 22 of 139**

Next

A 49-year-old female is admitted to hospital due to shortness of breath and pleuritic chest pain. She also complains of a marked decrease in appetite for the past 4 months. An admission chest x-ray shows a right-sided pleural effusion. An underlying malignancy is suspected and a series of tumour markers are requested:

CA 19-9	55 u/ml (< 40)
CA 125	654 u/ml (< 30)
CA 15-3	9 u/ml (<40)

What is the most likely underlying diagnosis?

- ☐ A. Ovarian fibroma
- ☐ B. Small cell lung cancer
- ☐ C. Pancreatic carcinoma
- ☐ D. Hepatocellular cancer
- ☐ E. Breast carcinoma

Next question

This patient has Meig's syndrome - an ovarian fibroma associated with a pleural effusion and ascites

**Tumour markers**

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

**Monoclonal antibodies**

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

**Tumour antigens**

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer



**Question 23 of 139**

Next

A 12-year-old boy is noted to bleed excessively during an elective dental extraction. Following the procedure, examination reveals petechial skin haemorrhages. Blood results show:

Hb	12.3 g/dl
Plt	$255 \times 10^9/l$
WBC	$7.9 \times 10^9/l$
PT	13.3 secs
APTT	39 secs
Factor VIII activity	87%

What is the most likely diagnosis?

- ☐ A. Disseminated intravascular coagulation
- ☐ B. Idiopathic thrombocytopenic purpura
- ☐ C. Von Willebrand's disease
- ☐ D. Haemophilia A
- ☐ E. Haemophilia B

Next question

The combination of a petechial skin rash combined with a slightly elevated APTT and reduced factor VIII activity make Von Willebrand's disease the most likely diagnosis

**Von Willebrand's disease**

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion\* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemarthroses and muscle haematomas are rare

**Role of von Willebrand factor**

- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

**Types**

- type 1: partial reduction in vWF (80% of patients)

- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

### Investigation

- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

### Management

- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

\*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

**Question 24 of 139**

Next

A 52-year-old woman with a history of hypothyroidism presents with lethargy and a sore tongue. Blood tests are reported as follows:

Hb	10.7 g/dl
MCV	121 fl
Plt	$177 \times 10^9/l$
WBC	$5.4 \times 10^9/l$

Further tests are ordered:

Vitamin B12	64 ng/l (200-900 ng/l)
Folic acid	7.2 nmol/l (> 3.0 nmol/l)

What is the most appropriate management?

- ☐ A. 1 mg of IM hydroxocobalamin once every 3 months
- ☐ B. 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months
- ☐ C. 1 mg of IM hydroxocobalamin once every 2 months + folic acid 5mg od
- ☐ D. Give folic acid 5mg od one week then recheck bloods
- ☐ E. 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months + folic acid 5mg od

Next question

If the patient was deficient in folic acid it would be important to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord.

**Vitamin B12 deficiency**

Vitamin B12 is mainly used in the body for red blood cell development and also maintenance of the nervous system. It is absorbed after binding to intrinsic factor (secreted from parietal cells in the stomach) and is actively absorbed in the terminal ileum. A small amount of vitamin B12 is passively absorbed without being bound to intrinsic factor.

Causes of vitamin B12 deficiency

- pernicious anaemia
- post gastrectomy
- poor diet
- disorders of terminal ileum (site of absorption): Crohn's, blind-loop etc

## Features of vitamin B12 deficiency

- macrocytic anaemia
- sore tongue and mouth
- neurological symptoms: e.g. Ataxia
- neuropsychiatric symptoms: e.g. Mood disturbances

## Management

- if no neurological involvement 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months
- if a patient is also deficient in folic acid then it is important to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord

A 54-year-old man is diagnosed as having acute myeloid leukaemia. What is the single most important test in determining his prognosis?

<input type="radio"/>	A. Gene-expression profiling
<input type="radio"/>	B. White cell count at diagnosis
<input type="radio"/>	C. Immunophenotyping
<input type="radio"/>	D. Lactate dehydrogenase
<input type="radio"/>	E. Cytogenetics

[Next question](#)

All of the above may be important but chromosomal abnormalities detected by cytogenetics are the single most important prognostic factor.

### Acute myeloid leukaemia

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Poor prognostic features

- > 60 years
- > 20% blasts after first course of chemo
- cytogenetics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3

- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)

- M0 - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic
- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic

A patient with a history of recurrent thromboembolic events develops a deep vein thrombosis despite full anticoagulation with heparin. Which one of the following causes of thrombophilia is associated with resistance to heparin?

<input type="radio"/>	A. Protein S deficiency
<input type="radio"/>	B. Antithrombin III deficiency
<input type="radio"/>	C. Protein C deficiency
<input type="radio"/>	D. Lupus anticoagulant
<input type="radio"/>	E. Activated protein C resistance

[Next question](#)

Heparin works by binding to antithrombin III, enhancing its anticoagulant effect by inhibiting the formation of thrombin and other clotting factors. Patients with antithrombin III deficiency may therefore be resistant to heparin treatment

### Antithrombin III deficiency

Antithrombin III deficiency is an inherited cause of thrombophilia occurring in approximately 1:2,000 of the population. Inheritance is autosomal dominant

Antithrombin III inhibits several clotting factors, primarily thrombin, factor X and factor IX. It mediates the effects of heparin

Antithrombin III deficiency comprises a heterogeneous group of disorders, with some patients having a deficiency of normal antithrombin III whilst others produce abnormal antithrombin III

#### Features

- recurrent venous thromboses
- arterial thromboses do occur but is uncommon

#### Management

- thromboembolic events are treated with lifelong warfarinisation
- heparinisation during pregnancy\*
- antithrombin III concentrates (often used during surgery or childbirth)

\*as patients with antithrombin III deficiency have a degree of resistance to heparin anti-Xa levels should be monitored carefully to ensure adequate anticoagulation

**Question 27 of 139**

Next

A 67-year-old woman is reviewed 6 months after she had a mastectomy following a diagnosis of breast cancer. Which one of the following tumour markers is most useful in monitoring her disease?

- ☐ A. CA 125
- ☐ B. CD 34
- ☐ C. CA 15-3
- ☐ D. CA 19-9
- ☐ E. CD 117

**Tumour markers**

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

**Monoclonal antibodies**

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

**Tumour antigens**

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

**Question 28 of 139**

Next

A 49-year-old woman is referred to the haematology clinic with easy bruising and recurrent epistaxis. She is otherwise well. Blood tests reveal the following:

Hb	12.9 g/dl
Platelets	$19 \times 10^9/l$
WCC	$6.6 \times 10^9/l$

The patient refuses consent for a bone marrow examination. What is the most appropriate initial management?

- ☐ A. Platelet transfusion
- ☐ B. Oral prednisolone
- ☐ C. No treatment
- ☐ D. ABVD chemotherapy
- ☐ E. Splenectomy

Next question

ITP - give oral prednisolone

The likely diagnosis in this patient is idiopathic thrombocytopenic purpura. The first line treatment in such patients is high-dose prednisolone. Bone marrow examination would demonstrate increased megakaryocytes

**ITP: investigation and management**

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex

**Investigations**

- antiplatelet autoantibodies (usually IgG)
- bone marrow aspiration shows megakaryocytes in the marrow. This should be carried out prior to the commencement of steroids in order to rule out leukaemia

**Management**

- oral prednisolone (80% of patients respond)
- splenectomy if platelets  $< 30$  after 3 months of steroid therapy
- IV immunoglobulins
- immunosuppressive drugs e.g. cyclophosphamide



**Question 29 of 139**

Next

A 71-year-old woman who is known to have multiple myeloma is admitted with confusion. Blood tests show the following:

Corrected calcium	2.91 mmol/l
-------------------	-------------

Which one of the following is the most significant cause of the raised calcium level?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Adverse effects of standard treatment        |
| <input type="radio"/> | B. Increased osteoclastic activation            |
| <input type="radio"/> | C. Impaired renal function                      |
| <input type="radio"/> | D. Increased renal tubular calcium reabsorption |
| <input type="radio"/> | E. Elevated PTH-rP levels                       |

Next question

**Myeloma: features**

Multiple myeloma is a neoplasm of the bone marrow plasma cells. The peak incidence is patients aged 60-70 years.

**Clinical features**

- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

Diagnosis is based on:

- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

**Hypercalcaemia in myeloma**

- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

What is the mechanism of action of DDAVP in von Willebrand's disease?

<input type="radio"/>	A. Prevents renal excretion of von Willebrand's factor
<input type="radio"/>	B. Promotes breakdown of large multimers
<input type="radio"/>	C. Induces release of von Willebrand's factor from endothelial cells
<input type="radio"/>	D. Inhibits breakdown of von Willebrand's factor
<input type="radio"/>	E. Acts as substitute carrier molecule for factor VIII

Next question

### Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion\* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemarthroses and muscle haematomas are rare

Role of von Willebrand factor

- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types

- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation

- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management

- tranexamic acid for mild bleeding

- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

\*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Which one of the following statements regarding the aetiology of venous thromboembolism (VTE) is correct?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Third generation combined oral contraceptive pills are safer than second generation ones |
| <input type="radio"/> | B. VTE develops in around 5% of patients with Goodpasture's syndrome                        |
| <input type="radio"/> | C. Female gender is a risk factor recurrent VTE   |
| <input type="radio"/> | D. The second trimester of pregnancy is associated with a greater risk than the puerperium  |
| <input type="radio"/> | E. Tamoxifen therapy increases the risk of VTE  |

Next question

### Venous thromboembolism: risk factors

Common predisposing factors include malignancy, pregnancy and the period following an operation. The comprehensive list below is partly based on the 2010 SIGN venous thromboembolism (VTE) guidelines:

#### General

- increased risk with advancing age
- obesity
- family history of VTE
- pregnancy (especially puerperium)
- immobility
- hospitalisation
- anaesthesia
- central venous catheter: femoral >> subclavian

#### Underlying conditions

- malignancy
- thrombophilia: e.g. Activated protein C resistance, protein C and S deficiency
- heart failure
- antiphospholipid syndrome
- Behcet's
- polycythaemia
- nephrotic syndrome
- sickle cell disease
- paroxysmal nocturnal haemoglobinuria
- hyperviscosity syndrome
- homocystinuria

## Medication

- combined oral contraceptive pill: 3rd generation more than 2nd generation
- hormone replacement therapy
- raloxifene and tamoxifen
- antipsychotics (especially olanzapine) have recently been shown to be a risk factor

SIGN also state that the following are risk factors for recurrent VTE:

- previous unprovoked VTE
- male sex
- obesity
- thrombophilias

What is the mechanism of action of cisplatin?

- ☐ A. Stabilises DNA-topoisomerase II complex
- ☐ B. Causes cross-linking in DNA
- ☐ C. Inhibits ribonucleotide reductase
- ☐ D. Inhibits purine synthesis
- ☐ E. Inhibits formation of microtubules

Next question

### Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

**Question 33 of 139**

Next

A 72-year-old man is admitted with a deep vein thrombosis. He is normally fit and well but has recently lost weight. Blood tests reveal the following:

IgG	889 mg/dl (range 600-1300 mg/dl)
IgM	1674 mg/dl (range 50-330 mg/dl)
IgA	131 mg/dl (range 60-300 mg/dl)

What is the most likely diagnosis?

- ☐ A. Monoclonal gammopathy of undetermined significance
- ☐ B. Acute promyelocytic leukaemia
- ☐ C. Waldenstrom's macroglobulinaemia
- ☐ D. Antiphospholipid syndrome
- ☐ E. Multiple myeloma

Next question

IgM paraproteinaemia - ?Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is more likely than monoclonal gammopathy of undetermined significance given the weight loss and deep vein thrombosis (evidence of hyperviscosity).

IgG and IgA are the most common type of immunoglobulins produced in myeloma.

**Waldenstrom's macroglobulinaemia**

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

**Features**

- monoclonal IgM paraproteinaemia
- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Which of the following is most associated with thymomas?

<input type="radio"/>	A. Myelodysplasia
<input type="radio"/>	B. Thrombocytopenia
<input type="radio"/>	C. Acute myeloid leukaemia
<input type="radio"/>	D. Acute lymphoblastic leukaemia
<input type="radio"/>	E. Red cell aplasia

Next question

## Thymoma

Thymomas are the most common tumour of the anterior mediastinum

Associated with

- myasthenia gravis (30-40% of patients with thymoma)
- red cell aplasia
- dermatomyositis
- also : SLE, SIADH

Causes of death

- compression of airway
- cardiac tamponade



Which of the following is a cause of extravascular haemolysis?

<input type="radio"/>	A. Hereditary spherocytosis
<input type="radio"/>	B. Paroxysmal nocturnal haemoglobinuria
<input type="radio"/>	C. Disseminated intravascular coagulation
<input type="radio"/>	D. Mismatched blood transfusion
<input type="radio"/>	E. Haemolytic uraemic syndrome

Next question

### Haemolytic anaemias: by site

In intravascular haemolysis free haemoglobin is released which binds to haptoglobin. As haptoglobin becomes saturated haemoglobin binds to albumin forming methaemalbumin (detected by Schumm's test). Free haemoglobin is excreted in the urine as haemoglobinuria, haemosiderinuria

Intravascular haemolysis: causes

- mismatched blood transfusion
- G6PD deficiency\*
- red cell fragmentation: heart valves, TTP, DIC, HUS
- paroxysmal nocturnal haemoglobinuria
- cold autoimmune haemolytic anaemia

Extravascular haemolysis: causes

- haemoglobinopathies: sickle cell, thalassaemia
- hereditary spherocytosis
- haemolytic disease of newborn
- warm autoimmune haemolytic anaemia

\*strictly speaking there is an element of extravascular haemolysis in G6PD as well, although it is usually classified as a intravascular cause

**Question 36 of 139**

Next

A 65-year-old woman is reviewed. She is on the waiting list for a varicose vein operation but during the preoperative assessment was noted to have a raised lymphocyte count. She reports feeling well currently and clinical examination is normal. Her bloods were as follows:

Hb	11.8 g/dl
Plt	$184 \times 10^9/l$
WBC	$21.2 \times 10^9/l$

There are no previous bloods to compare these results with. Following referral to haematology a diagnosis of chronic lymphocytic leukaemia was made. What is the most appropriate management?

- ☐ A. No treatment + cancel operation
- ☐ B. No treatment + go ahead with operation
- ☐ C. Chlorambucil + cancel operation
- ☐ D. Fludarabine + go ahead with operation but with quinolone prophylaxis
- ☐ E. Alemtuzumab + cancel operation

Next question

There is no indication for treating this patient at the current time or not going ahead with surgery

**Chronic lymphocytic leukaemia: management****Indications for treatment**

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (>10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38°C for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopenias e.g. ITP

**Management**

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients

**Question 37 of 139**

Next

A 73-year-old woman is reviewed in the pre-op clinic prior to an elective hip replacement. Her past medical history includes polymyalgia rheumatica and ischaemic heart disease. Screening blood tests are ordered and the full blood count is reported as follows:

Hb	12.9 g/dl
Plt	$158 \times 10^9/l$
WBC	$19.0 \times 10^9/l$
Neuts	$4.2 \times 10^9/l$
Lymphs	$14.1 \times 10^9/l$

What is the most likely diagnosis?

- ☐ A. Lymphoma
- ☐ B. Nicorandil-related lymphocytosis
- ☐ C. Transient viral illness
- ☐ D. Chronic lymphocytic leukaemia
- ☐ E. Secondary to steroid use

Such a lymphocytosis in an elderly patient is very likely to be caused by chronic lymphocytic leukaemia. Steroids tend to cause a neutrophilia. It would be unusual for a viral illness to cause such a marked lymphocytosis in an elderly person.

**Chronic lymphocytic leukaemia**

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

Features

- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

Complications

- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

Investigations

- blood film: smudge cells
- immunophenotyping

**Question 38 of 139**

Next

A 67-year-old man is diagnosed with myelofibrosis. What is the most common presenting symptom of myelofibrosis?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Lethargy                 |
| <input type="radio"/> | B. Anorexia and weight loss |
| <input type="radio"/> | C. Night sweats             |
| <input type="radio"/> | D. Easy bruising            |
| <input type="radio"/> | E. Splenomegaly             |

Next question

Myelofibrosis - most common presenting symptom - lethargy

Whilst all the above may be seen in myelofibrosis lethargy is the most common

**Myelofibrosis**

## Overview

- a myeloproliferative disorder
- thought to be caused by hyperplasia of abnormal megakaryocytes
- the resultant release of platelet derived growth factor is thought to stimulate fibroblasts
- haematopoiesis develops in the liver and spleen

## Features

- e.g. elderly person with symptoms of anaemia e.g. fatigue (the most common presenting symptom)
- massive splenomegaly
- hypermetabolic symptoms: weight loss, night sweats etc

## Laboratory findings

- anaemia
- high WBC and platelet count early in the disease
- 'tear-drop' poikilocytes on blood film
- unobtainable bone marrow biopsy - 'dry tap' therefore trephine biopsy needed
- high urate and LDH (reflect increased cell turnover)

Which one of the following malignancies may be associated with HTLV-1?

<input type="radio"/>	A. Adult T-cell leukaemia
<input type="radio"/>	B. Colorectal cancer
<input type="radio"/>	C. Burkitt's lymphoma
<input type="radio"/>	D. Medullary thyroid cancer
<input type="radio"/>	E. Breast cancer

Next question

### Haematological malignancies: infections

#### Viruses

- EBV: Hodgkin's and Burkitt's lymphoma, nasopharyngeal carcinoma
- HTLV-1: Adult T-cell leukaemia/lymphoma
- HIV-1: High-grade B-cell lymphoma

#### Bacteria

- *Helicobacter pylori*: gastric lymphoma (MALT)

#### Protozoa

- malaria: Burkitt's lymphoma

Each one of the following may cause eosinophilia, except:

<input type="radio"/>	A. Allergic bronchopulmonary aspergillosis
<input type="radio"/>	B. Extrinsic allergic alveolitis
<input type="radio"/>	C. Churg-Strauss syndrome
<input type="radio"/>	D. Psoriasis
<input type="radio"/>	E. Toxocara infection

Next question

## Eosinophilia

Causes of eosinophilia may be divided into pulmonary, infective and other

Pulmonary causes

- asthma
- allergic bronchopulmonary aspergillosis
- Churg-Strauss syndrome
- Löffler's syndrome
- tropical pulmonary eosinophilia
- eosinophilic pneumonia
- hypereosinophilic syndrome

Infective causes

- schistosomiasis
- nematodes: Toxocara, Ascaris, Strongyloides
- cestodes: Echinococcus

Other causes

- drugs: sulfasalazine, nitrofurantoin
- psoriasis/eczema
- eosinophilic leukaemia (very rare)

A 51-year-old female is referred to the haematology clinic with a haemoglobin of 19.2 g/dl. She is a non-smoker. Her oxygen saturations on room air are 98% and she is noted to have mass in the left upper quadrant. What is the most useful test to establish whether she has polycythaemia rubra vera?

<input type="radio"/>	A. Bone marrow aspiration
<input type="radio"/>	B. Blood film
<input type="radio"/>	C. Red cell mass
<input type="radio"/>	D. Transferrin saturation
<input type="radio"/>	E. JAK2 mutation screen

[Next question](#)

Polycythaemia rubra vera - JAK2 mutation

The discovery of the JAK2 mutation has made red cell mass a second-line investigation for patients with suspected JAK2-negative polycythaemia rubra vera

### Polycythaemia rubra vera: features

Polycythaemia rubra vera (PRV) is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with PRV and this has resulted in significant changes to the diagnostic criteria. The incidence of PRV peaks in the sixth decade.

#### Features

- hyperviscosity
- pruritus, typically after a hot bath
- splenomegaly
- haemorrhage (secondary to abnormal platelet function)
- plethoric appearance
- hypertension in a third of patients

Following history and examination, the British Committee for Standards in Haematology (BCSH) recommend the following tests are performed

- full blood count/film (raised haematocrit; neutrophils, basophils, platelets raised in half of patients)
- JAK2 mutation
- serum ferritin
- renal and liver function tests

If the JAK2 mutation is negative and there is no obvious secondary causes the BCSH suggest the following tests:

- red cell mass
- arterial oxygen saturation
- abdominal ultrasound
- serum erythropoietin level
- bone marrow aspirate and trephine
- cytogenetic analysis
- erythroid burst-forming unit (BFU-E) culture

Other features that may be seen in PRV include a low ESR and a raised leukocyte alkaline phosphatase

The diagnostic criteria for PRV have recently been updated by the BCSH. This replaces the previous PRV Study Group criteria.

JAK2-positive PRV - diagnosis requires both criteria to be present

A1	High haematocrit (>0.52 in men, >0.48 in women) OR raised red cell mass (>25% above predicted)
A2	Mutation in JAK2

JAK2-negative PRV - diagnosis requires A1 + A2 + A3 + either another A or two B criteria

A1	Raised red cell mass (>25% above predicted) OR haematocrit >0.60 in men, >0.56 in women
A2	Absence of mutation in JAK2
A3	No cause of secondary erythrocytosis
A4	Palpable splenomegaly
A5	Presence of an acquired genetic abnormality (excluding BCR-ABL) in the haematopoietic cells
B1	Thrombocytosis (platelet count $>450 \times 10^9/l$ )
B2	Neutrophil leucocytosis (neutrophil count $> 10 \times 10^9/l$ in non-smokers; $> 12.5 \times 10^9/l$ in smokers)
B3	Radiological evidence of splenomegaly
B4	Endogenous erythroid colonies or low serum erythropoietin



Which one of the following translocations is associated with acute promyelocytic leukaemia?

- |                       |             |
|-----------------------|-------------|
| <input type="radio"/> | A. t(15;17) |
| <input type="radio"/> | B. t(9;17)  |
| <input type="radio"/> | C. t(9;22)  |
| <input type="radio"/> | D. t(15;22) |
| <input type="radio"/> | E. t(17;22) |

Next question

Acute promyelocytic leukaemia - t(15;17)

### Acute promyelocytic leukaemia

You are not normally expected to be able to differentiate the different subtypes of acute myeloid leukaemia (AML) for the MRCP. An exception to this is acute promyelocytic leukaemia (APML, the M3 subtype of AML). The importance of identifying APML lies in both the presentation (classically disseminated intravascular coagulation) and management

APML is associated with the t(15;17) translocation which causes fusion of the PML and RAR-alpha genes.

#### Features

- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Which one of the following features is least recognised in thrombotic thrombocytopenic purpura?

<input type="radio"/>	A. Fever
<input type="radio"/>	B. Microangiopathic haemolytic anaemia
<input type="radio"/>	C. Renal failure
<input type="radio"/>	D. Thrombocytopenia
<input type="radio"/>	E. Livedo reticularis

Next question

Livedo reticularis is not commonly seen in thrombotic thrombocytopenic purpura. It occurs more commonly in conditions such as antiphospholipid syndrome and cholesterol embolism

### Thrombotic thrombocytopenic purpura

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of caspase which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Features

- rare, typically adult females
- fever
- fluctuating neuro signs (microemboli)
- microangiopathic haemolytic anaemia
- thrombocytopenia
- renal failure

Causes

- post-infection e.g. urinary, gastrointestinal
- pregnancy
- drugs: ciclosporin, oral contraceptive pill, penicillin, clopidogrel, aciclovir
- tumours
- SLE
- HIV

Which one of the following ethnic groups have an increased incidence of prostate cancer?

<input type="radio"/>	A. Afro-Caribbean
<input type="radio"/>	B. Ashkenazi Jews
<input type="radio"/>	C. Chinese
<input type="radio"/>	D. Indian subcontinent
<input type="radio"/>	E. White

Next question

### Prostate cancer: features

Prostate cancer is the second most common cancer in adult males in the UK and is the most common malignant condition in men over 65 years.

#### Risk factors

- increasing age
- Afro-Caribbean ethnicity

#### Features

- bladder outlet obstruction: hesitancy, urinary retention
- haematuria, haematospermia
- pain: back, perineal or testicular
- digital rectal examination: asymmetrical, hard, nodular enlargement with loss of median sulcus

Which one of the following viruses is associated with nasopharyngeal carcinoma?

<input type="radio"/>	A. Adenovirus
<input type="radio"/>	B. Rhinovirus
<input type="radio"/>	C. Herpes simplex virus
<input checked="" type="radio"/>	D. Epstein-Barr virus
<input type="radio"/>	E. Picornavirus

Next question

EBV: associated malignancies:

- Burkitt's lymphoma
- Hodgkin's lymphoma
- nasopharyngeal carcinoma

### Epstein-Barr virus: associated conditions

Malignancies associated with EBV infection

- Burkitt's lymphoma\*
- Hodgkin's lymphoma
- nasopharyngeal carcinoma
- HIV-associated central nervous system lymphomas

The non-malignant condition hairy leukoplakia is also associated with EBV infection.

\*EBV is currently thought to be associated with both African and sporadic Burkitt's

Which one of the following would most suggest a leukaemoid reaction rather than chronic myeloid leukaemia?

<input type="radio"/>	A. Raised packed cell volume
<input type="radio"/>	B. Right shift of neutrophils
<input type="radio"/>	C. A low leucocyte alkaline phosphatase score
<input type="radio"/>	D. Dohle bodies in the white cells
<input type="radio"/>	E. Positive osmotic fragility test

Next question

### Leukaemoid reaction

The leukaemoid reaction describes the presence of immature cells such as myeloblasts, promyelocytes and nucleated red cells in the peripheral blood. This may be due to infiltration of the bone marrow causing the immature cells to be 'pushed out' or sudden demand for new cells

#### Causes

- severe infection
- severe haemolysis
- massive haemorrhage
- metastatic cancer with bone marrow infiltration

A relatively common clinical problem is differentiating chronic myeloid leukaemia from a leukaemoid reaction. The following differences may help:

#### Leukaemoid reaction

- high leucocyte alkaline phosphatase score
- toxic granulation (Dohle bodies) in the white cells
- 'left shift' of neutrophils i.e. three or less segments of the nucleus

#### Chronic myeloid leukaemia

- low leucocyte alkaline phosphatase score

**Question 47 of 139**

Next

A 62-year-old man presents with lethargy. A full blood count is taken and is reported as follows:

Hb	10.2 g/dl
Platelets	$330 \times 10^9/l$
WBC	$15.2 \times 10^9/l$
Film	Leucoerythroblastic picture. Tear-drop poikilocytes seen

What is the most likely diagnosis?

- ☐ A. Myelodysplasia
- ☐ B. Chronic lymphocytic leukaemia
- ☐ C. Myelofibrosis
- ☐ D. Chronic myeloid leukaemia
- ☐ E. Post-splenectomy

Next question

Tear-drop poikilocytes = myelofibrosis

Thrombocytopenia and leucopenia are seen in progressive disease

**Blood films: typical pictures**

Hyposplenism e.g. post-splenectomy

- target cells
- Howell-Jolly bodies
- Pappenheimer bodies
- siderotic granules
- acanthocytes
- schizocytes

Iron-deficiency anaemia

- target cells
- 'pencil' poikilocytes
- if combined with B12/folate deficiency a 'dimorphic' film occurs with mixed microcytic and macrocytic cells

## Myelofibrosis

- 'tear-drop' poikilocytes

## Intravascular haemolysis

- schistocytes

## Megaloblastic anaemia

- hypersegmented neutrophils

**Question 48 of 139**

Next

A 24-year-old nulliparous female with a history of recurrent deep vein thrombosis presents with shortness of breath. The full blood count and clotting screen reveals the following results:

Hb	12.4 g/dl
Plt	137
WBC	$7.5 \times 10^9/l$
PT	14 secs
APTT	46 secs

What is the most likely underlying diagnosis?

- ☐ A. Third generation oral contraceptive pill use
- ☐ B. Protein C deficiency
- ☐ C. Antithrombin III deficiency
- ☐ D. Antiphospholipid syndrome
- ☐ E. Activated protein C resistance

Next question

Antiphospholipid syndrome: (paradoxically) prolonged APTT + low platelets

The combination of a prolonged APTT and thrombocytopenia make antiphospholipid syndrome the most likely diagnosis

**Antiphospholipid syndrome**

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

**Features**

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis



- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

#### Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

#### Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

A 73-year-old man is prescribed cetuximab after being diagnosed with metastatic colorectal cancer. What target is this monoclonal antibody directed against?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Vascular endothelial growth factor receptor |
| <input type="radio"/> | B. Angiopoietin-2 receptors                    |
| <input type="radio"/> | C. CD20 protein complex                        |
| <input type="radio"/> | D. Epidermal growth factor receptor            |
| <input type="radio"/> | E. Fibroblast growth factor receptor           |

[Next question](#)

Cetuximab - monoclonal antibody against the epidermal growth factor receptor

### Monoclonal antibodies

Monoclonal antibodies have an increasing role in medicine. They are manufactured by a technique called somatic cell hybridization. This involves the fusion of myeloma cells with spleen cells from a mouse that has been immunized with the desired antigen. The resulting fused cells are termed a hybridoma and act as a 'factory' for producing monoclonal antibodies. The main limitation to this is that mouse antibodies are immunogenic leading to the formation of human anti-mouse antibodies (HAMAs). This problem is overcome by combining the variable region from the mouse body with the constant region from a human antibody.

Clinical examples of monoclonal antibodies:

- infliximab (anti-TNF): used in rheumatoid arthritis and Crohn's
- rituximab (anti-CD20): used in non-Hodgkin's lymphoma and rheumatoid arthritis
- cetuximab (anti epidermal growth factor receptor): used in metastatic colorectal cancer and head and neck cancer
- trastuzumab (anti-HER2, an EGF receptor): used in metastatic breast cancer
- alemtuzumab (anti-CD52): used in chronic lymphocytic leukaemia
- abciximab (anti-glycoprotein IIb/IIIa receptor): prevention of ischaemic events in patients undergoing percutaneous coronary interventions
- OKT3 (anti-CD3): used to prevent organ rejection

Monoclonal antibodies are also used for:

- medical imaging when combined with a radioisotope
- identification of cell surface markers in biopsied tissue
- diagnosis of viral infections

**Question 50 of 139**

Next

A 34-year-old female presents due to the development of a purpuric rash on the back of her legs. Her only regular medication is Microgynon 30. She also reports frequent nose bleeds and menorrhagia. A full blood count is requested:

Hb	11.7 g/dl
Platelets	$62 \times 10^9/l$
WCC	$5.3 \times 10^9/l$
PT	11 secs
APTT	30 secs
Factor VIIIc activity	Normal

What is the most likely diagnosis?

<input type="radio"/>	A. Drug-induced thrombocytopenia
<input type="radio"/>	B. Henoch-Schonlein purpura
<input type="radio"/>	C. Thrombotic thrombocytopenic purpura
<input type="radio"/>	D. Idiopathic thrombocytopenic purpura
<input type="radio"/>	E. Antiphospholipid syndrome

Next question

The isolated thrombocytopenia in a well patient points to a diagnosis of ITP. The combined oral contraceptive pill does not commonly cause blood dyscrasias

**ITP**

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex.

ITP can be divided into acute and chronic forms:

**Acute ITP**

- more commonly seen in children
- equal sex incidence
- may follow an infection or vaccination
- usually runs a self-limiting course over 1-2 weeks

## Chronic ITP

- more common in young/middle-aged women
- tends to run a relapsing-remitting course

## Evan's syndrome

- ITP in association with autoimmune haemolytic anaemia (AIHA)

A 26-year-old man with a history of hereditary haemorrhagic telangiectasia is planning to start a family. What is the mode of inheritance?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Autosomal dominant with incomplete penetrance  |
| <input type="radio"/> | B. Autosomal codominant                           |
| <input type="radio"/> | C. Autosomal recessive with incomplete penetrance |
| <input type="radio"/> | D. Autosomal dominant                             |
| <input type="radio"/> | E. Autosomal recessive                            |

[Next question](#)

Hereditary haemorrhagic telangiectasia - autosomal dominant

### Hereditary haemorrhagic telangiectasia

Also known as Osler-Weber-Rendu syndrome, hereditary haemorrhagic telangiectasia (HHT) is an autosomal dominant condition characterised by (as the name suggests) multiple telangiectasia over the skin and mucous membranes. Twenty percent of cases occur spontaneously without prior family history.

There are 4 main diagnostic criteria. If the patient has 2 then they are said to have a possible diagnosis of HHT. If they meet 3 or more of the criteria they are said to have a definite diagnosis of HHT:

- epistaxis : spontaneous, recurrent nosebleeds
- telangiectases: multiple at characteristic sites (lips, oral cavity, fingers, nose)
- visceral lesions: for example gastrointestinal telangiectasia (with or without bleeding), pulmonary arteriovenous malformations (AVM), hepatic AVM, cerebral AVM, spinal AVM
- family history: a first-degree relative with HHT

A man is investigated for anaemia. A blood film is ordered and reported as follows:

Ring sideroblasts

Which one of the following is least likely to give this picture?

<input type="radio"/>	A. Anti-tuberculosis medication
<input type="radio"/>	B. Alcohol
<input type="radio"/>	C. Pyridoxine
<input type="radio"/>	D. Lead
<input type="radio"/>	E. Myelodysplasia

Next question

Pyridoxine is actually a treatment for sideroblastic anaemia. Rarely pyridoxine deficiency may be the cause

### Sideroblastic anaemia

Sideroblastic anaemia is a condition where red cells fail to completely form haem, whose biosynthesis takes place partly in the mitochondrion. This leads to deposits of iron in the mitochondria that form a ring around the nucleus called a ring sideroblast. It may be congenital or acquired

Congenital cause: delta-aminolevulinate synthase-2 deficiency

Acquired causes

- myelodysplasia
- alcohol
- lead
- anti-TB medications

Investigations

- hypochromic microcytic anaemia (more so in congenital)
- bone marrow: sideroblasts and increased iron stores

Management

- supportive
- treat any underlying cause
- pyridoxine may help

A 65-year-old man comes for review. He has a history of small cell lung cancer and ischaemic heart disease. His cancer was diagnosed five months ago and he has recently completed a course of chemotherapy. From a cardiac point of view he had a myocardial infarction two years ago following which he had primary angioplasty with stent placement. He has had no angina since.

For the past week he has become increasingly short-of-breath. This is worse at night and is associated with an occasional non-productive cough. He has also noticed that his wedding ring feels tight. Clinical examination of his chest is unremarkable. He does however have distended neck veins and periorbital oedema. What is the most likely diagnosis?

<input type="radio"/>	A. Heart failure secondary to chemotherapy
<input type="radio"/>	B. Tumour lysis syndrome
<input type="radio"/>	C. Nephrotic syndrome secondary to chemotherapy
<input type="radio"/>	D. Superior vena cava obstruction
<input type="radio"/>	E. Hypercalcaemia

[Next question](#)

### Superior vena cava obstruction

Superior vena cava (SVC) obstruction is an oncological emergency caused by compression of the SVC. It is most commonly associated with lung cancer.

#### Features

- dyspnoea is the most common symptom
- swelling of the face, neck and arms - conjunctival and periorbital oedema may be seen
- headache
- visual disturbance
- pulseless jugular venous distension

#### Causes

- common malignancies: small cell lung cancer, lymphoma
- other malignancies: metastatic seminoma, Kaposi's sarcoma, breast cancer
- aortic aneurysm
- mediastinal fibrosis
- goitre
- SVC thrombosis

## Management

- general: dexamethasone, balloon venoplasty, stenting
- small cell: chemotherapy + radiotherapy
- non-small cell: radiotherapy



**Question 54 of 139**

Next

A 35-year-old woman presents with menorrhagia and a persistent sore throat. A full blood count shows the following:

Hb	6.8 g/dl
Platelets	$45 \times 10^9/l$
WBC	$1.4 \times 10^9/l$
Neutrophils	$0.8 \times 10^9/l$

Which one of the following medications is most likely to account for this finding?

<input type="radio"/>	A. Trimethoprim
<input type="radio"/>	B. Rifampicin
<input type="radio"/>	C. Olanzapine
<input type="radio"/>	D. Montelukast
<input type="radio"/>	E. Clomifene

Next question

Trimethoprim may cause pancytopenia

**Drug-induced pancytopenia**

Drug causes of pancytopenia

- cytotoxics
- antibiotics: trimethoprim, chloramphenicol
- anti-rheumatoid: gold, penicillamine
- carbimazole\*
- anti-epileptics: carbamazepine
- sulphonylureas: tolbutamide

\*causes both agranulocytosis and pancytopenia

**Question 55 of 139**

Next

A 35-year-old female who is 34 weeks pregnant presents with a swollen, painful right calf. A deep vein thrombosis is confirmed on Doppler scan. What is the preferred anticoagulant?

<input type="radio"/>	A. Clopidogrel
<input type="radio"/>	B. Aspirin
<input type="radio"/>	C. Intravenous heparin
<input type="radio"/>	D. Warfarin
<input type="radio"/>	E. Subcutaneous low molecular weight heparin

Next question

Although teratogenic effects of warfarin are greater in the first trimester most clinicians would use low molecular weight heparin in this situation. Another factor to consider is the risk of peripartum haemorrhage and potential problems reversing the effects of warfarin if this occurred

**Pregnancy: DVT/PE**

## Overview

- pregnancy is a hypercoagulable state
- majority occur in last trimester

## Pathophysiology

- increase in factors VII, VIII, X and fibrinogen
- decrease in protein S
- uterus presses on IVC causing venous stasis in legs

## Management

- warfarin contraindicated
- S/C low-molecular weight heparin preferred to IV heparin (less bleeding and thrombocytopenia)

Which one of the following features is least recognised in myeloma?

<input type="radio"/>	A. Bone pain
<input type="radio"/>	B. Amyloidosis
<input type="radio"/>	C. Lethargy
<input type="radio"/>	D. Night sweats
<input type="radio"/>	E. Pathological fractures

Next question

Night sweats are a feature of non-Hodgkin's lymphoma

### Myeloma: features

Multiple myeloma is a neoplasm of the bone marrow plasma cells. The peak incidence is patients aged 60-70 years.

#### Clinical features

- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

Diagnosis is based on:

- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

#### Hypercalcaemia in myeloma

- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

**Question 57 of 139**

Next

A 67-year-old woman is referred to the haematology clinic. Her GP has noted that her platelet count is persistently elevated and no reactive cause can be found. Bloods taken a week before clinic are as follows:

Hb	15.4 g/dl
Platelets	$784 \times 10^9/l$
WBC	$5.3 \times 10^9/l$
JAK2 kinase (V617F mutation)	Positive

What is the treatment of choice?

- ☐ A. Imatinib
- ☐ B. Stem-cell transplantation
- ☐ C. Hydroxycarbamide
- ☐ D. Vincristine
- ☐ E. Venesection

Next question

**Thrombocytosis**

Thrombocytosis is an abnormally high platelet count, usually  $> 400 \times 10^9/l$ .

Causes of thrombocytosis

- reactive: platelets are an acute phase reactant - platelet count can increase in response to stress such as a severe infection or surgery
- malignancy
- essential thrombocytosis (see below), or as part of another myeloproliferative disorder such as chronic myeloid leukaemia or polycythaemia rubra vera
- hyposplenism

**Essential thrombocytosis**

Essential thrombocytosis is one of the myeloproliferative disorders which overlaps with chronic myeloid leukaemia, polycythaemia rubra vera and myelofibrosis. Megakaryocyte proliferation results in an overproduction of platelets.

Features

- platelet count  $> 600 \times 10^9/l$

- both thrombosis (venous or arterial) and haemorrhage can be seen
- a characteristic symptom is a burning sensation in the hands
- a JAK2 mutation is found in around 50% of patients

## Management

- hydroxyurea (hydroxycarbamide) is widely used to reduce the platelet count
- interferon- $\alpha$  is also used in younger patients
- low-dose aspirin may be used to reduce the thrombotic risk

A 74-year-old woman with a past history of chronic lymphocytic leukaemia presents with lethargy. The following blood results are obtained:

Hb	7.9 g/dl
Plt	$158 \times 10^9/l$
WCC	$24.0 \times 10^9/l$
Blood film:	normochromic, normocytic anaemia

What complication has most likely occurred?

- ☐ A. Paroxysmal nocturnal haemoglobinuria
- ☐ B. Microangiopathic haemolytic anaemia
- ☐ C. Sideroblastic anaemia
- ☐ D. Warm autoimmune haemolytic anaemia
- ☐ E. Cold autoimmune haemolytic anaemia

Next question

Warm autoimmune haemolytic anaemia occurs in around 10-15% of patients with chronic lymphocytic leukaemia

### Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

#### Features

- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

#### Complications

- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

#### Investigations

- blood film: smudge cells
- immunophenotyping

**Question 59 of 139**

Next

A 31-year-old man is referred to the acute medical unit with a painful swollen left leg. The patient reports that he has the 'Factor V Leiden mutation'. Which one of the following best describes the pathophysiology of his condition?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Protein S deficiency              |
| <input type="radio"/> | B. Activated protein C excess        |
| <input type="radio"/> | C. Antithrombin deficiency           |
| <input type="radio"/> | D. Resistance to action of protein C |
| <input type="radio"/> | E. Activated protein C deficiency    |

Next question

Factor V Leiden mutation results in activated protein C resistance

**Activated protein C resistance**

Activated protein C resistance is the most common inherited thrombophilia. It is due to a mutation in the Factor V Leiden mutation. Heterozygotes have a 5-fold risk of venous thrombosis whilst homozygotes have a 50-fold increased risk

Which of the following is a cause of intravascular haemolysis?

<input type="radio"/>	A. Hereditary spherocytosis
<input type="radio"/>	B. Sickle cell anaemia
<input type="radio"/>	C. Paroxysmal nocturnal haemoglobinuria
<input type="radio"/>	D. Haemolytic disease of the newborn
<input type="radio"/>	E. Warm autoimmune haemolytic anaemia

Next question

### Haemolytic anaemias: by site

In intravascular haemolysis free haemoglobin is released which binds to haptoglobin. As haptoglobin becomes saturated haemoglobin binds to albumin forming methaemalbumin (detected by Schumm's test). Free haemoglobin is excreted in the urine as haemoglobinuria, haemosiderinuria

Intravascular haemolysis: causes

- mismatched blood transfusion
- G6PD deficiency\*
- red cell fragmentation: heart valves, TTP, DIC, HUS
- paroxysmal nocturnal haemoglobinuria
- cold autoimmune haemolytic anaemia

Extravascular haemolysis: causes

- haemoglobinopathies: sickle cell, thalassaemia
- hereditary spherocytosis
- haemolytic disease of newborn
- warm autoimmune haemolytic anaemia

\*strictly speaking there is an element of extravascular haemolysis in G6PD as well, although it is usually classified as a intravascular cause



A 27-year-old male is receiving cyclophosphamide as part of his chemotherapy for non-Hodgkin' lymphoma. What is the most appropriate management to reduce the likelihood of haemorrhagic cystitis?

<input type="radio"/>	A. Hydration + tranexamic acid
<input type="radio"/>	B. Hydration + twice-daily bladder washouts
<input type="radio"/>	C. Hydration + prophylactic antibiotics
<input type="radio"/>	D. Hydration + twice-daily bladder washouts + prophylactic antibiotics
<input type="radio"/>	E. Hydration + mesna

[Next question](#)

Cyclophosphamide - haemorrhagic cystitis - prevent with mesna

Cyclophosphamide may be converted to urotoxic metabolites such as acrolein. Mesna binds to these metabolites through its sulfhydryl-moieties and reduces the incidence of haemorrhagic cystitis

### Cyclophosphamide

Cyclophosphamide is an alkylating agent used in the management of cancer and autoimmune conditions. It works by causing cross-linking of DNA

#### Adverse effects

- haemorrhagic cystitis: incidence reduced by the use of hydration and mesna
- myelosuppression
- transitional cell carcinoma

**Question 62 of 139**

Next

A 31-year-old woman who is 25-weeks pregnant is brought to the Emergency Department by her husband. Over the past two days she has become increasingly confused. Her temperature is 37.8°C and blood pressure is 104/62 mmHg. Blood tests show:

Hb	8.3 g/dl
Platelets	$88 \times 10^9/l$
WBC	$15.1 \times 10^9/l$
Blood film	Fragmented red blood cells
Sodium	139 mmol/l
Potassium	5.2 mmol/l
Urea	19.4 mmol/l
Creatinine	296 $\mu$ mol/l

What is the most appropriate treatment?

<input type="radio"/>	A. Rituximab
<input type="radio"/>	B. Intravenous immunoglobulin
<input type="radio"/>	C. Methylprednisolone
<input type="radio"/>	D. Ceftriaxone + vancomycin
<input type="radio"/>	E. Plasma exchange

TTP - plasma exchange is first-line

This patient has thrombotic thrombocytopenic purpura, a condition associated with pregnancy

**Thrombotic thrombocytopenic purpura: management**

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of protease which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Management

- no antibiotics - may worsen outcome
- plasma exchange is the treatment of choice
- steroids, immunosuppressants
- vincristine

A 54-year-old woman presents to the Emergency Department with a five day history of back pain. Her past medical history includes breast cancer and osteoarthritis. The back pain is located in the lower thoracic region and is made worse by coughing and sneezing. There has been no change in bowel habit or urinary symptoms. On examination there is diffuse tenderness in the lower thoracic region. Peri-anal sensation is normal and lower limb reflexes are brisk. Which one of the following is the most appropriate management plan?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Organise outpatient MRI                                 |
| <input type="radio"/> | B. Oral paracetamol + urgent MRI                           |
| <input type="radio"/> | C. Oral paracetamol + urgent thoracic/lumbar spine x-ray   |
| <input type="radio"/> | D. Oral dexamethasone + urgent thoracic/lumbar spine x-ray |
| <input type="radio"/> | E. Oral dexamethasone + urgent MRI                         |

[Next question](#)

This woman has spinal cord compression until proven otherwise and should have urgent assessment.

Recent NICE guidelines suggest contacting the local metastatic spinal cord compression coordinator in this situation. This should hopefully prevent delays in treatment by ensuring the patient is admitted to the most appropriate place

### Spinal cord compression

Spinal cord compression is an oncological emergency and affects up to 5% of cancer patients. Extradural compression accounts for the majority of cases, usually due to vertebral body metastases. It is more common in patients with lung, breast and prostate cancer

#### Features

- back pain - the earliest and most common symptom - may be worse on lying down and coughing
- lower limb weakness
- sensory changes: sensory loss and numbness
- neurological signs depend on the level of the lesion. Lesions above L1 usually result in upper motor neuron signs in the legs and a sensory level. Lesions below L1 usually cause lower motor neuron signs in the legs and perianal numbness. Tendon reflexes tend to be increased below the level of the lesion and absent at the level of the lesion

#### Management

- high-dose oral dexamethasone
- urgent oncological assessment for consideration of radiotherapy or surgery

What is the most common inherited bleeding disorder?

<input type="radio"/>	A. Haemophilia A
<input type="radio"/>	B. Activated protein C resistance
<input type="radio"/>	C. Haemophilia B
<input type="radio"/>	D. Antithrombin III deficiency
<input type="radio"/>	E. von Willebrand's disease

Next question

### Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion\* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemarthroses and muscle haematomas are rare

Role of von Willebrand factor

- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

Types

- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

Investigation

- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

Management

- tranexamic acid for mild bleeding

- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

\*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Which one of the following is not an indication for treatment in chronic lymphocytic leukaemia?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Massive splenomegaly                   |
| <input type="radio"/> | B. Platelet count of $77 \times 10^9/l$   |
| <input type="radio"/> | C. Night sweats                           |
| <input type="radio"/> | D. Lymphocyte count of $65 \times 10^9/l$ |
| <input type="radio"/> | E. Extreme fatigue                        |

Next question

The absolute lymphocyte count is not an indication for treatment, rather than the rate of increase (see guidelines below)

### Chronic lymphocytic leukaemia: management

#### Indications for treatment

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive (>10 cm) or progressive lymphadenopathy
- massive (>6 cm) or progressive splenomegaly
- progressive lymphocytosis: > 50% increase over 2 months or lymphocyte doubling time < 6 months
- systemic symptoms: weight loss > 10% in previous 6 months, fever >38°C for > 2 weeks, extreme fatigue, night sweats
- autoimmune cytopaenias e.g. ITP

#### Management

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients

A 45-year-old man known to have haemochromatosis attends for blood test to assess when he next needs venesection. Of the options given, which one of the following blood tests should be used to assess the adequacy of venesection?

<input type="radio"/>	A. Ferritin
<input type="radio"/>	B. Serum iron
<input type="radio"/>	C. Haemoglobin
<input type="radio"/>	D. Total iron binding capacity
<input type="radio"/>	E. Haematocrit

[Next question](#)

The British Committee for Standards in Haematology recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

### Haemochromatosis: investigation

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6\*. The British Committee for Standards in Haematology (BCSH) published guidelines for the investigation and management of haemochromatosis in 2000

There is continued debate about the best investigation to screen for haemochromatosis. The 2000 BCSH guidelines suggest:

- general population: transferrin saturation is considered the most useful marker. Ferritin should also be measured but is not usually abnormal in the early stages of iron accumulation
- testing family members: genetic testing for HFE mutation

These guidelines may change as HFE gene analysis become less expensive

#### Diagnostic tests

- molecular genetic testing for the C282Y and H63D mutations
- liver biopsy: Perl's stain

#### Typical iron study profile in patient with haemochromatosis

- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

Monitoring adequacy of venesection

- BSCH recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Joint x-rays characteristically show chondrocalcinosis

\*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene



A 64-year-old man is reviewed in the haematology clinic. Which one of the following features would suggest that a diagnosis monoclonal gammopathy of undetermined significance is more likely than myeloma?

<input type="radio"/>	A. Bone pain
<input type="radio"/>	B. IgG paraprotein band = 18g/l
<input type="radio"/>	C. Creatinine = 160 $\mu$ mol/l
<input type="radio"/>	D. Raised beta-2 microglobulin
<input type="radio"/>	E. Lytic lesions on x-ray

[Next question](#)

Paraproteinaemia is seen in both myeloma and monoclonal gammopathy of undetermined significance (MGUS) - at this level a diagnosis of MGUS is more likely. The other features indicate myeloma

### MGUS

Monoclonal gammopathy of undetermined significance (MGUS, also known as benign paraproteinaemia and monoclonal gammopathy) is a common condition that causes a paraproteinaemia and is often mistaken for myeloma. Differentiating features are listed below. Around 10% of patients eventually develop myeloma at 5 years, with 50% at 15 years

#### Features

- usually asymptomatic
- no bone pain or increased risk of infections
- around 10-30% of patients have a demyelinating neuropathy

#### Differentiating features from myeloma

- normal immune function
- normal beta-2 microglobulin levels
- lower level of paraproteinaemia than myeloma (e.g. < 30g/l IgG, or < 20g/l IgA)
- stable level of paraproteinaemia
- no clinical features of myeloma (e.g. lytic lesions on x-rays or renal disease)

What is the most useful marker of prognosis in myeloma?

- ☐ A. Calcium level
- ☐ B. Urine Bence-Jones protein levels
- ☐ C. Alkaline phosphatase
- ☐ D. ESR
- ☐ E. B2-microglobulin

Next question

### Myeloma: prognosis

B2-microglobulin is a useful marker of prognosis - raised levels imply poor prognosis. Low levels of albumin are also associated with a poor prognosis

### International prognostic index

Stage	Criteria	Median survival (months)
I	B2 microglobulin < 3.5 mg/l Albumin > 35 g/l	62
II	Not I or III	45
III	B2 microglobulin > 5.5 mg/l	29

Regarding the Ann-Arbor classification of Hodgkin's lymphoma, which one of the following would be staged as IIIB?

<input type="radio"/>	A. Nodes on both sides of diaphragm with pruritus
<input type="radio"/>	B. Two or more lymph nodes on the same side of the diaphragm with pruritus
<input type="radio"/>	C. Nodes on both sides of diaphragm with night sweats
<input type="radio"/>	D. Two or more lymph nodes on the same side of the diaphragm with night sweats
<input type="radio"/>	E. Two or more lymph nodes on the same side of the diaphragm with no systemic symptoms

[Next question](#)

### Hodgkin's lymphoma: staging

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

Ann-Arbor staging of Hodgkin's lymphoma

- I: single lymph node
- II: 2 or more lymph nodes/regions on same side of diaphragm
- III: nodes on both sides of diaphragm
- IV: spread beyond lymph nodes

Each stage may be subdivided into A or B

- A = no systemic symptoms other than pruritus
- B = weight loss > 10% in last 6 months, fever > 38c, night sweats (poor prognosis)

Which one of the following is the most common type of Hodgkin's lymphoma?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Lymphocyte predominant |
| <input type="radio"/> | B. Nodular sclerosing     |
| <input type="radio"/> | C. Lymphocyte depleted    |
| <input type="radio"/> | D. Mixed cellularity      |
| <input type="radio"/> | E. Hairy cell             |

Next question

Hodgkin's lymphoma - most common type = nodular sclerosing

### Hodgkin's lymphoma: histological classification and prognosis

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

#### Histological classification

- nodular sclerosing: most common, good prognosis
- mixed cellularity: good prognosis
- lymphocyte predominant: best prognosis
- lymphocyte depleted: least common, worst prognosis

'B' symptoms also imply a poor prognosis

- weight loss > 10% in last 6 months
- fever > 38°C
- night sweats

Other factors associated with a poor prognosis identified in a 1998 NEJM paper included:

- age > 45 years
- stage IV disease
- haemoglobin < 10.5 g/dl
- lymphocyte count < 600/ $\mu$ l or < 8%
- male
- albumin < 40 g/l
- white blood count > 15,000/ $\mu$ l

**Question 71 of 139**

Next

A 62-year-old man is called for review after a positive faecal occult blood test done as part of the national screening programme. During counselling for colonoscopy he asks what percentage of patients with a positive faecal occult blood test have colorectal cancer. What is the most accurate answer?

- |                       |             |
|-----------------------|-------------|
| <input type="radio"/> | A. 0.5 - 2% |
| <input type="radio"/> | B. 5 - 15%  |
| <input type="radio"/> | C. 20 - 30% |
| <input type="radio"/> | D. 30 - 50% |
| <input type="radio"/> | E. 55 - 75% |

Next question

Colorectal cancer screening - PPV of FOB = 5 - 15%

There is also a 30-45% chance of having an adenoma with a positive faecal occult blood test

**Colorectal cancer: screening****Overview**

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screening programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligible patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cancer

Which of the following is a good prognostic factor in chronic lymphocytic leukaemia?

<input type="radio"/>	A. Female sex
<input type="radio"/>	B. Lymphocyte doubling time < 12 months
<input type="radio"/>	C. CD38 expression positive
<input type="radio"/>	D. Age > 70 years
<input type="radio"/>	E. Raised LDH

Next question

### Chronic lymphocytic leukaemia: prognostic factors

Poor prognostic factors (median survival 3-5 years)

- male sex
- age > 70 years
- lymphocyte count > 50
- prolymphocytes comprising more than 10% of blood lymphocytes
- lymphocyte doubling time < 12 months
- raised LDH
- CD38 expression positive

What are the most common types of transformations seen in patients with polycythaemia rubra vera?

- |                                  |   |
|----------------------------------|---|
| <input type="radio"/>            | A. Myelodysplasia + chronic myeloid leukaemia |
| <input type="radio"/>            | B. Myelofibrosis + chronic myeloid leukaemia  |
| <input type="radio"/>            | C. Myelodysplasia + myelofibrosis             |
| <input checked="" type="radio"/> | D. Myelofibrosis + acute myeloid leukaemia    |
| <input type="radio"/>            | E. Myelodysplasia + acute myeloid leukaemia   |

Next question

Polycythaemia rubra vera - around 5-15% progress to myelofibrosis or AML

### Polycythaemia rubra vera: management

Polycythaemia rubra vera is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets.. It has peak incidence in the sixth decade, with typical features including hyperviscosity, pruritus and splenomegaly

#### Management

- venesection - first line treatment
- hydroxyurea -slight increased risk of secondary leukaemia
- phosphorus-32 therapy

#### Prognosis

- thrombotic events are a significant cause of morbidity and mortality
- 5-15% of patients progress to myelofibrosis
- 5-15% of patients progress to acute leukaemia (risk increased with chemotherapy treatment)

A 54-year-old female is receiving a course of chemotherapy for breast cancer. She is experiencing troublesome vomiting which has not been helped by domperidone. What is the most appropriate next management step?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. Add an antihistamine               |
| <input type="radio"/> | B. Add a 5HT2 antagonist              |
| <input type="radio"/> | C. Add a phenothiazine                |
| <input type="radio"/> | D. Add a dopamine receptor antagonist |
| <input type="radio"/> | E. Add a 5HT3 antagonist              |

[Next question](#)

### Chemotherapy side-effects: nausea and vomiting

Nausea and vomiting are common side-effects of chemotherapy. Risk factors for the development of symptoms include:

- anxiety
- age less than 50 years old
- concurrent use of opioids
- the type of chemotherapy used

For patients at low-risk of symptoms then drugs such as metoclopramide may be used first-line. For high-risk patients then 5HT3 receptor antagonists such as ondansetron are often effective, especially if combined with dexamethasone



Each one of the following is associated with iron-deficiency anaemia, except:

<input type="radio"/>	A. Atrophic glossitis
<input type="radio"/>	B. Onycholysis
<input type="radio"/>	C. Post-cricoid webs
<input type="radio"/>	D. Koilonychia
<input type="radio"/>	E. Angular stomatitis

Next question

## Iron deficiency anaemia

### Features

- koilonychia
- atrophic glossitis
- post-cricoid webs
- angular stomatitis

### Blood film

- target cells
- 'pencil' poikilocytes
- if combined with B12/folate deficiency a 'dimorphic' film occurs with mixed microcytic and macrocytic cells

**Question 76 of 139**

Next

A 50-year-old woman is investigated for weight loss and anaemia. She has no past medical history of note. Clinical examination reveals splenomegaly associated with pale conjunctivae. A full blood count is reported as follows:

Hb	10.9 g/dl
Platelets	$702 \times 10^9/l$
WCC	$56.6 \times 10^9/l$
Film	Leucocytosis noted. All stages of granulocyte maturation seen

Given the likely diagnosis, what is the most appropriate treatment?

- ☐ A. Chlorambucil
- ☐ B. Stem cell transplantation
- ☐ C. Rituximab
- ☐ D. Repeat full blood count in 3 months
- ☐ E. Imatinib

Next question

**Chronic myeloid leukaemia**

The Philadelphia chromosome is present in more than 95% of patients with chronic myeloid leukaemia (CML). It is due to a translocation between the long arm of chromosome 9 and 22 - t(9:22)(q34; q11). This results in part of the ABL proto-oncogene from chromosome 9 being fused with the BCR gene from chromosome 22. The resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal

Presentation (40-50 years)

- middle-age
- anaemia, weight loss, abdo discomfort
- splenomegaly may be marked
- spectrum of myeloid cells seen in peripheral blood
- decreased neutrophil alkaline phosphatase
- may undergo blast transformation (AML in 80%, ALL in 20%)

Management

- imatinib is now considered first-line treatment
- hydroxyurea
- interferon-alpha

- allogenic bone marrow transplant

## Imatinib

- inhibitor of the tyrosine kinase associated with the BCR-ABL defect
- very high response rate in chronic phase CML

Burkitt's lymphoma is associated with a mutation in which one of the following genes?

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. Cyclin D1 gene |
| <input type="radio"/> | B. PML gene       |
| <input type="radio"/> | C. BCR-ABL gene   |
| <input type="radio"/> | D. RAR-alpha gene |
| <input type="radio"/> | E. MYC gene       |

Next question

### Haematological malignancies: genetics

Below is a brief summary of the common translocations associated with haematological malignancies

t(9;22) - Philadelphia chromosome

- present in > 95% of patients with CML
- this results in part of the Abelson proto-oncogene being moved to the BCR gene on chromosome 22
- the resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal
- poor prognostic indicator in ALL

t(15;17)

- seen in acute promyelocytic leukaemia (M3)
- fusion of PML and RAR-alpha genes

t(8;14)

- seen in Burkitt's lymphoma
- MYC oncogene is translocated to an immunoglobulin gene

t(11;14)

- Mantle cell lymphoma
- deregulation of the cyclin D1 (BCL-1) gene

**Question 78 of 139**

Next

A 18-year-old man who is known to have hereditary spherocytosis is admitted to hospital with lethargy. Admission bloods show the following:

Hb	4.7 g/dl
Retics	0.3%

What is the most likely explanation for these findings?

- ☐ A. Haemolytic crisis
- ☐ B. Recent ciprofloxacin therapy
- ☐ C. Parvovirus infection
- ☐ D. Sequestration crises
- ☐ E. Angiodysplastic bowel lesions

Next question

This man has had an aplastic crisis secondary to parvovirus infection.

**Hereditary spherocytosis****Basics**

- most common hereditary haemolytic anaemia in people of northern European descent
- autosomal dominant defect of red blood cell cytoskeleton
- the normal biconcave disc shape is replaced by a sphere-shaped red blood cell
- red blood cell survival reduced as destroyed by the spleen

**Presentation**

- failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable

**Diagnosis**

- osmotic fragility test

**Management**

- folate replacement
- splenectomy

**Question 79 of 139**

Next

A 23-year-old woman presents with lethargy. The following blood results are obtained:

Hb	10.4 g/dl
Plt	$278 \times 10^9/l$
WCC	$6.3 \times 10^9/l$
MCV	68 fl
Blood film	Microcytic hypochromic RBCs, marked anisocytosis and basophilic stippling noted
HbA2	3.9%

What is the most likely diagnosis?

- ☐ A. Lead poisoning
- ☐ B. Sickle cell anaemia
- ☐ C. Beta-thalassaemia trait
- ☐ D. Hereditary spherocytosis
- ☐ E. Sideroblastic anaemia

Next question

Disproportionate microcytic anaemia - think beta-thalassaemia trait

A microcytic anaemia in a female should raise the possibility of either gastrointestinal blood loss or menorrhagia. However, there is no history to suggest this and the microcytosis is disproportionately low for the haemoglobin level. This combined with a raised HbA2 points to a diagnosis of beta-thalassaemia trait.

Basophilic stippling is also seen in lead poisoning but would not explain the raised HbA2 levels.

**Beta-thalassaemia trait**

The thalassaemias are a group of genetic disorders characterised by a reduced production rate of either alpha or beta chains. Beta-thalassaemia trait is an autosomal recessive condition characterised by a mild hypochromic, microcytic anaemia. It is usually asymptomatic

**Features**

- mild hypochromic, microcytic anaemia - microcytosis is characteristically disproportionate to the anaemia
- HbA2 raised ( $> 3.5\%$ )

A patient presents as she has a strong family history of cancer. Which one of the following cancers is least likely to be inherited?

<input type="radio"/>	A. Colorectal cancer
<input type="radio"/>	B. Breast cancer
<input type="radio"/>	C. Gastric cancer
<input type="radio"/>	D. Endometrial cancer
<input type="radio"/>	E. Ovarian cancer

Between 5 and 10% of all breast cancers are thought to be hereditary. Mutation in the BRCA1 and BRCA2 genes also increase the risk of ovarian cancer. For colorectal cancer around 5% of cases are caused by hereditary non-polyposis colorectal carcinoma (HNPCC) and 1% are due to familial adenomatous polyposis. Women who have HNPCC also have a markedly increased risk for developing endometrial cancer - around 5% of endometrial cancers occur in women with this risk factor.

### Cancer in the UK

The most common causes of cancer in the UK are as follows\*

- 1. Breast
- 2. Lung
- 3. Colorectal
- 4. Prostate
- 5. Bladder
- 6. Non-Hodgkin's lymphoma
- 7. Melanoma
- 8. Stomach
- 9. Oesophagus
- 10. Pancreas

The most common causes of death from cancer in the UK are as follows:

- 1. Lung
- 2. Colorectal
- 3. Breast
- 4. Prostate
- 5. Pancreas
- 6. Oesophagus
- 7. Stomach
- 8. Bladder
- 9. Non-Hodgkin's lymphoma
- 10. Ovarian

\*excludes non-melanoma skin cancer

A 72-year-old man is diagnosed with prostate cancer and goserelin (Zoladex) is prescribed. Which one of the following is it most important to co-prescribe for the first three weeks of treatment?

<input type="radio"/>	A. Tamoxifen
<input type="radio"/>	B. Lansoprazole
<input type="radio"/>	C. Allopurinol
<input type="radio"/>	D. Cyproterone acetate
<input type="radio"/>	E. Tamsulosin

Anti-androgen treatment such as cyproterone acetate should be co-prescribed when starting gonadorelin analogues due to the risk of tumour flare. This phenomenon is secondary to initial stimulation of luteinising hormone release by the pituitary gland resulting in increased testosterone levels.

The BNF advises starting cyproterone acetate 3 days before the gonadorelin analogue.

### Prostate cancer: management

#### Localised prostate cancer (T1/T2)

Treatment depends on life expectancy and patient choice. Options include:

- conservative: active monitoring & watchful waiting
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

#### Localised advanced prostate cancer (T3/T4)

Options include:

- hormonal therapy: see below
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

#### Metastatic prostate cancer disease - hormonal therapy

Synthetic GnRH agonist

- e.g. Goserelin (Zoladex)
- cover initially with anti-androgen to prevent rise in testosterone

Anti-androgen

- cyproterone acetate prevents DHT binding from intracytoplasmic protein complexes

Orchidectomy



A woman is prescribed docetaxel as part of her chemotherapy for breast cancer. What is the mechanism of action of docetaxel?

- ☐ A. Inhibits RNA synthesis
- ☐ B. Stabilizes DNA-topoisomerase II complex
- ☐ C. Prevents microtubule disassembly
- ☐ D. Inhibits formation of microtubules
- ☐ E. Causes cross-linking in DNA

Taxanes (e.g. Docetaxel) prevent microtubule disassembly

Like other taxanes the principal mechanism of action is the prevention of microtubule disassembly.

### Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis
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Next

### Question 83 of 139

A 58-year-old man is reviewed in clinic. Six months ago he had a Whipple procedure for pancreatic cancer and is currently undergoing chemotherapy. Which one of the following blood tests is most useful in monitoring his disease?

- ☐ A. CA 15-3 levels
- ☐ B. Faecal elastase
- ☐ C. CA 125 levels
- ☐ D. Amylase levels
- ☐ E. CA 19-9 levels

[Next question](#)

### Tumour markers

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

### Monoclonal antibodies

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

### Tumour antigens

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma

Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

**Question 84 of 139**

A patient is due to start chemotherapy for metastatic colorectal cancer. What is the main advantage of using capecitabine instead of fluorouracil?

- ☐ A. Current data shows increased survival
- ☐ B. Less cardiotoxic
- ☐ C. Oral administration
- ☐ D. Less nausea
- ☐ E. Not renally excreted therefore can be used in patients with chronic kidney disease

[Next question](#)

Capecitabine is an orally administered prodrug which is enzymatically converted to 5-fluorouracil in the tumour.

**Cytotoxic agents**

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

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Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

Which one of the following is least associated with hepatocellular carcinoma?

<input type="radio"/>	A. Hepatitis C
<input type="radio"/>	B. Primary biliary cirrhosis
<input type="radio"/>	C. Aflatoxin
<input type="radio"/>	D. Wilson's disease
<input type="radio"/>	E. Haemochromatosis

Next question

### Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is the third most common cause of cancer worldwide. Chronic hepatitis B is the most common cause of HCC worldwide with chronic hepatitis C being the most common cause in Europe.

The main risk factor for developing HCC is liver cirrhosis, for example secondary\* to hepatitis B & C, alcohol, haemochromatosis and primary biliary cirrhosis. Other risk factors include:

- alpha-1 antitrypsin deficiency
- hereditary tyrosinosis
- glycogen storage disease
- aflatoxin
- drugs: oral contraceptive pill, anabolic steroids
- porphyria cutanea tarda
- male sex
- diabetes mellitus, metabolic syndrome

### Features

- tends to present late
- features of liver cirrhosis or failure may be seen: jaundice, ascites, RUQ pain, hepatomegaly, pruritus, splenomegaly
- possible presentation is decompensation in a patient with chronic liver disease

Screening with ultrasound (+/- alpha-fetoprotein) should be considered for high risk groups such as:

- patients liver cirrhosis secondary to hepatitis B & C or haemochromatosis
- men with liver cirrhosis secondary to alcohol

## Management options

- early disease: surgical resection
- liver transplantation
- radiofrequency ablation
- transarterial chemoembolisation
- sorafenib: a multikinase inhibitor

\*Wilson's disease is an exception

A 30-year-old man enquires about screening for haemochromatosis as his brother was diagnosed with the condition 2 years ago. The patient is currently well with no features suggestive of haemochromatosis. What is the most appropriate investigation?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Serum total iron-binding capacity |
| <input type="radio"/> | B. HFE gene analysis                 |
| <input type="radio"/> | C. Serum transferrin saturation      |
| <input type="radio"/> | D. Serum ferritin                    |
| <input type="radio"/> | E. Serum iron                        |

[Next question](#)

#### Screening for haemochromatosis

- general population: transferrin saturation > ferritin
- family members: HFE genetic testing

Serum transferrin saturation is currently the preferred investigation for population screening. However, the patient has a sibling with haemochromatosis and therefore HFE gene analysis is the most suitable investigation. In clinical practice this would be combined with iron studies as well

#### Haemochromatosis: investigation

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6\*. The British Committee for Standards in Haematology (BCSH) published guidelines for the investigation and management of haemochromatosis in 2000

There is continued debate about the best investigation to screen for haemochromatosis. The 2000 BCSH guidelines suggest:

- general population: transferrin saturation is considered the most useful marker. Ferritin should also be measured but is not usually abnormal in the early stages of iron accumulation
- testing family members: genetic testing for HFE mutation

These guidelines may change as HFE gene analysis become less expensive

#### Diagnostic tests

- molecular genetic testing for the C282Y and H63D mutations



- liver biopsy: Perl's stain

Typical iron study profile in patient with haemochromatosis

- transferrin saturation > 55% in men or > 50% in women
- raised ferritin (e.g. > 500 ug/l) and iron
- low TIBC

Monitoring adequacy of venesection

- BSCH recommend 'transferrin saturation should be kept below 50% and the serum ferritin concentration below 50 ug/l'

Joint x-rays characteristically show chondrocalcinosis

\*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

Your review a 41-year-old woman. Four months ago she developed a deep vein thrombosis and was warfarinised with a target INR of 2.5. She has presented with a swollen, tender left calf and a Doppler scan confirms a further deep vein thrombosis. Her INR has been above 2.0 for the past three months. You organise some investigations to exclude an underlying prothrombotic condition. What should happen regarding her anticoagulation?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Switch to treatment dose low-molecular weight heparin |
| <input type="radio"/> | B. Continue on warfarin, continue with INR target of 2.5 |
| <input type="radio"/> | C. Add aspirin 75 mg od                                  |
| <input type="radio"/> | D. Continue on warfarin, increase INR target to 3.0      |
| <input type="radio"/> | E. Continue on warfarin, increase INR target to 3.5      |

[Next question](#)

## Warfarin

Warfarin is an oral anticoagulant which inhibits the reduction of vitamin K to its active hydroquinone form, which in turn acts as a cofactor in the formation of clotting factor II, VII, IX and X (mnemonic = 1972) and protein C .

### Indications

- venous thromboembolism: target INR = 2.5, if recurrent 3.5
- atrial fibrillation, target INR = 2.5
- mechanical heart valves, target INR depends on the valve type and location. Mitral valves generally require a higher INR than aortic valves.

Patients on warfarin are monitored using the INR (international normalised ratio), the ratio of the prothrombin time for the patient over the normal prothrombin time. Warfarin has a long half-life and achieving a stable INR may take several days. There a variety of loading regimes and computer software is now often used to alter the dose.

### Factors that may potentiate warfarin

- liver disease
- P450 enzyme inhibitors, e.g.: amiodarone, ciprofloxacin
- cranberry juice
- drugs which displace warfarin from plasma albumin, e.g. NSAIDs
- inhibit platelet function: NSAIDs

### Side-effects

- haemorrhage
- teratogenic, although can be used in breast-feeding mothers
- skin necrosis: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis
- purple toes

Which one of the following is least associated with thrombocytopenia?

<input type="radio"/>	A. Heparin therapy
<input type="radio"/>	B. Rheumatoid arthritis
<input type="radio"/>	C. Infectious mononucleosis
<input type="radio"/>	D. Liver disease
<input type="radio"/>	E. Pregnancy

Next question

Rheumatoid arthritis, unlike systemic lupus erythematosus, is generally associated with a thrombocytosis. In some cases of Felty's syndrome thrombocytopenia may be seen secondary to hypersplenism. This however represents a small percentage of patients with rheumatoid arthritis

### Thrombocytopenia

Causes of severe thrombocytopenia

- ITP
- DIC
- TTP
- haematological malignancy

Causes of moderate thrombocytopenia

- heparin induced thrombocytopenia (HIT)
- drug-induced (e.g. quinine, diuretics, sulphonamides, aspirin, thiazides)
- alcohol
- liver disease
- hypersplenism
- viral infection (EBV, HIV, hepatitis)
- pregnancy
- SLE/antiphospholipid syndrome
- vitamin B12 deficiency

A 43-year-old woman is about to start treatment with trastuzumab for metastatic breast cancer. What is the most important investigation to perform prior to initiating treatment?

<input type="radio"/>	A. Pulmonary function tests
<input checked="" type="radio"/>	B. Echo
<input type="radio"/>	C. Liver function tests
<input type="radio"/>	D. Chest x-ray
<input type="radio"/>	E. Glucose tolerance test

[Next question](#)

Trastuzumab (Herceptin) - cardiac toxicity is common

### Trastuzumab

Trastuzumab (Herceptin) is a monoclonal antibody directed against the HER2/neu receptor. It is used mainly in metastatic breast cancer although some patients with early disease are now also given trastuzumab.

#### Adverse effects

- flu-like symptoms and diarrhoea are common
- cardiotoxicity: more common when anthracyclines have also been used. An echo is usually performed before starting treatment

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A 61-year-old presents for review. She has been having atypical lower back pain for the past two months. An x-ray of her lumbar spine reported raised the possibility of spinal metastases but there is no current evidence of a primary tumour. A series of tumour markers were sent. Which one of the following is most associated with raised levels of CA 15-3?

- ☐ A. Pancreatic cancer
- ☐ B. Colorectal cancer
- ☐ C. Breast cancer
- ☐ D. Ovarian cancer
- ☐ E. Hepatocellular carcinoma

**Tumour markers**

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

**Monoclonal antibodies**

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

**Tumour antigens**

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

## Question 91 of 139

Which one of the following is least associated with eosinophilia?

<input type="radio"/>	A. Churg-Strauss syndrome
<input type="radio"/>	B. Nematode infection
<input type="radio"/>	C. Histoplasmosis
<input type="radio"/>	D. Allergic bronchopulmonary aspergillosis
<input type="radio"/>	E. Asthma

[Next question](#)

### Eosinophilia

Causes of eosinophilia may be divided into pulmonary, infective and other

Pulmonary causes

- asthma
- allergic bronchopulmonary aspergillosis
- Churg-Strauss syndrome
- Löffler's syndrome
- tropical pulmonary eosinophilia
- eosinophilic pneumonia
- hypereosinophilic syndrome

Infective causes

- schistosomiasis
- nematodes: Toxocara, Ascaris, Strongyloides
- cestodes: Echinococcus

Other causes

- drugs: sulfasalazine, nitrofurantoin
- psoriasis/eczema
- eosinophilic leukaemia (very rare)

Which one of the following haematological disorders is most associated with gingival hyperplasia?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Chronic lymphocytic leukaemia |
| <input type="radio"/> | B. Myelofibrosis                 |
| <input type="radio"/> | C. Polycythaemia rubra vera      |
| <input type="radio"/> | D. Haemophilia A                 |
| <input type="radio"/> | E. Acute myeloid leukaemia       |

Next question

Gingival hyperplasia: phenytoin, ciclosporin, calcium channel blockers and AML

### Gingival hyperplasia

Drug causes of gingival hyperplasia

- phenytoin
- ciclosporin
- calcium channel blockers (especially nifedipine)

Other causes of gingival hyperplasia include

- acute myeloid leukaemia (myelomonocytic and monocytic types)



Which one of the following is least associated with small cell lung cancer?

<input type="radio"/>	A. Bad prognosis
<input type="radio"/>	B. Cushing's syndrome
<input type="radio"/>	C. PTH-related peptide secretion
<input type="radio"/>	D. Hyponatraemia
<input type="radio"/>	E. Lambert-Eaton syndrome

#### Paraneoplastic features of lung cancer

- squamous cell: PTHrp, clubbing, HPOA
- small cell: ADH, ACTH, Lambert-Eaton syndrome

PTH-related peptide secretion is seen in squamous cell lung cancer

#### Lung cancer: small cell

##### Features

- usually central
- arise from APUD\* cells
- associated with ectopic ADH, ACTH secretion
- ADH --> hyponatraemia
- ACTH --> Cushing's syndrome
- ACTH secretion can cause bilateral adrenal hyperplasia, the high levels of cortisol can lead to hypokalaemic alkalosis
- Lambert-Eaton syndrome: antibodies to voltage gated calcium channels causing myasthenic like syndrome

##### Management

- usually metastatic disease by time of diagnosis
- surgery: only used for debulking
- most patients with limited disease now receive a combination of chemotherapy and radiotherapy
- patients with more extensive disease are offered palliative chemotherapy

\*an acronym for

- Amine - high amine content
- Precursor Uptake - high uptake of amine precursors
- Decarboxylase - high content of the enzyme decarboxylase

Each one of the following is associated with hyposplenism, except:

<input type="radio"/>	A. Sickle-cell anaemia
<input type="radio"/>	B. Liver cirrhosis
<input type="radio"/>	C. Systemic lupus erythematosus
<input type="radio"/>	D. Coeliac disease
<input type="radio"/>	E. Splenectomy

Next question

## Hyposplenism

### Causes

- splenectomy
- sickle-cell
- coeliac disease, dermatitis herpetiformis
- Graves' disease
- systemic lupus erythematosus
- amyloid

### Features

- Howell-Jolly bodies
- siderocytes

A 72-year-old man is referred to haematology with a raised haemoglobin. A diagnosis of polycythaemia rubra vera is suspected. Which other abnormality of the blood would be most consistent with this diagnosis?

<input type="radio"/>	A. Raised alkaline phosphatase
<input type="radio"/>	B. Hypokalaemia
<input type="radio"/>	C. Thrombocytopaenia
<input type="radio"/>	D. Raised ferritin level
<input type="radio"/>	E. Neutrophilia

[Next question](#)

### Polycythaemia rubra vera: features

Polycythaemia rubra vera (PRV) is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with PRV and this has resulted in significant changes to the diagnostic criteria. The incidence of PRV peaks in the sixth decade.

#### Features

- hyperviscosity
- pruritus, typically after a hot bath
- splenomegaly
- haemorrhage (secondary to abnormal platelet function)
- plethoric appearance
- hypertension in a third of patients

Following history and examination, the British Committee for Standards in Haematology (BCSH) recommend the following tests are performed

- full blood count/film (raised haematocrit; neutrophils, basophils, platelets raised in half of patients)
- JAK2 mutation
- serum ferritin
- renal and liver function tests

If the JAK2 mutation is negative and there is no obvious secondary causes the BCSH suggest the following tests:

- red cell mass
- arterial oxygen saturation

- abdominal ultrasound
- serum erythropoietin level
- bone marrow aspirate and trephine
- cytogenetic analysis
- erythroid burst-forming unit (BFU-E) culture

Other features that may be seen in PRV include a low ESR and a raised leukocyte alkaline phosphatase

The diagnostic criteria for PRV have recently been updated by the BCSH. This replaces the previous PRV Study Group criteria.

JAK2-positive PRV - diagnosis requires both criteria to be present

A1	High haematocrit (>0.52 in men, >0.48 in women) OR raised red cell mass (>25% above predicted)
A2	Mutation in JAK2

JAK2-negative PRV - diagnosis requires A1 + A2 + A3 + either another A or two B criteria

A1	Raised red cell mass (>25% above predicted) OR haematocrit >0.60 in men, >0.56 in women
A2	Absence of mutation in JAK2
A3	No cause of secondary erythrocytosis
A4	Palpable splenomegaly
A5	Presence of an acquired genetic abnormality (excluding BCR-ABL) in the haematopoietic cells
B1	Thrombocytosis (platelet count $>450 \times 10^9/l$ )
B2	Neutrophil leucocytosis (neutrophil count $> 10 \times 10^9/l$ in non-smokers; $> 12.5 \times 10^9/l$ in smokers)
B3	Radiological evidence of splenomegaly
B4	Endogenous erythroid colonies or low serum erythropoietin

Which of the following factors is associated with a good prognosis in acute myeloid leukaemia?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Translocation between chromosome 9 and 14        |
| <input type="radio"/> | B. Translocation between chromosome 15 and 17       |
| <input type="radio"/> | C. 25% blast following first course of chemotherapy |
| <input type="radio"/> | D. Deletion of chromosome 5                         |
| <input type="radio"/> | E. Deletion of chromosome 7                         |

Next question

Acute myeloid leukaemia - good prognosis: t(15;17)

A translocation between chromosome 15 and 17 is seen in acute promyelocytic leukaemia, which is known to carry a good prognosis

### Acute myeloid leukaemia

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Poor prognostic features

- > 60 years
- > 20% blasts after first course of chemo
- cytogenetics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3

- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)

- M0 - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic

- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic

Which one of the following haematological malignancies is most commonly associated with the t(11;14) translocation?

<input type="radio"/>	A. Acute promyelocytic leukaemia
<input type="radio"/>	B. Burkitt's lymphoma
<input type="radio"/>	C. Acute lymphoblastic leukaemia
<input type="radio"/>	D. Mantle cell lymphoma
<input type="radio"/>	E. Chronic myeloid leukaemia

[Next question](#)

### Haematological malignancies: genetics

Below is a brief summary of the common translocations associated with haematological malignancies

t(9;22) - Philadelphia chromosome

- present in > 95% of patients with CML
- this results in part of the Abelson proto-oncogene being moved to the BCR gene on chromosome 22
- the resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal
- poor prognostic indicator in ALL

t(15;17)

- seen in acute promyelocytic leukaemia (M3)
- fusion of PML and RAR-alpha genes

t(8;14)

- seen in Burkitt's lymphoma
- MYC oncogene is translocated to an immunoglobulin gene

t(11;14)

- Mantle cell lymphoma
- deregulation of the cyclin D1 (BCL-1) gene

Which one of the following therapeutic options is least recognised in the treatment of aplastic anaemia?

<input type="radio"/>	A. Interferon-alpha
<input type="radio"/>	B. Stem cell transplantation
<input type="radio"/>	C. Anti-lymphocyte globulin
<input type="radio"/>	D. Anti-thymocyte globulin
<input type="radio"/>	E. Platelet transfusion

Next question

### Aplastic anaemia: management

#### Supportive

- blood products
- prevention and treatment of infection

#### Anti-thymocyte globulin (ATG) and anti-lymphocyte globulin (ALG)

- prepared in animals (e.g. rabbits or horses) by injecting human lymphocytes
- is highly allergenic and may cause serum sickness (fever, rash, arthralgia), therefore steroid cover usually given
- immunosuppression using agents such as ciclosporin may also be given

#### Stem cell transplantation

- allogeneic transplants have a success rate of up to 80%



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Next

A 15-year-old girl is referred to haematology. She started having periods three years ago which have always been heavy and prolonged. Unfortunately the menorrhagia has responded poorly to trials of tranexamic acid and the combined oral contraceptive pill. Blood tests show the following:

Hb	10.3 g/dl
Plt	$239 \times 10^9/l$
WBC	$6.5 \times 10^9/l$
PT	12.9 secs
APTT	37 secs

What is the most likely diagnosis?

<input type="radio"/>	A. Haemophilia B
<input type="radio"/>	B. Disseminated intravascular coagulation
<input type="radio"/>	C. Haemophilia A
<input type="radio"/>	D. Idiopathic thrombocytopenic purpura
<input type="radio"/>	E. Von Willebrand's disease

Next question

Von Willebrand's disease is the most likely diagnosis as it is the most common inherited bleeding disorder. The mildly elevated APTT is consistent with this diagnosis.

The mild anaemia is consistent with the long history of menorrhagia.

**Von Willebrand's disease**

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion\* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemarthroses and muscle haematomas are rare

**Role of von Willebrand factor**

- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

**Types**

- type 1: partial reduction in vWF (80% of patients)

- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

### Investigation

- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

### Management

- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

\*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Which one of the following is least recognised as a treatment modality in idiopathic thrombocytopenic purpura?

<input type="radio"/>	A. Plasma exchange
<input type="radio"/>	B. Splenectomy
<input type="radio"/>	C. IV immunoglobulin
<input type="radio"/>	D. Cyclophosphamide
<input type="radio"/>	E. Oral prednisolone

Next question

### ITP: investigation and management

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex

#### Investigations

- antiplatelet autoantibodies (usually IgG)
- bone marrow aspiration shows megakaryocytes in the marrow. This should be carried out prior to the commencement of steroids in order to rule out leukaemia

#### Management

- oral prednisolone (80% of patients respond)
- splenectomy if platelets < 30 after 3 months of steroid therapy
- IV immunoglobulins
- immunosuppressive drugs e.g. cyclophosphamide

**Question 101 of 139**

Next

An 80-year-old man is reviewed in the haematology clinic. He has been referred due to weight loss, lethargy and a significantly elevated IgM level. Recent bloods show the following:

Hb	13.8 g/dl
Platelets	$127 \times 10^9/l$
IgM	2150 mg/dl (range 50-330 mg/dl)
ESR	45 mm/hr

Given the likely diagnosis, which one of the following complications is he most likely to develop?

- ☐ A. Renal failure
- ☐ B. Chronic lymphocytic leukaemia
- ☐ C. Anaemia
- ☐ D. Hyperviscosity syndrome
- ☐ E. Hypercalcaemia

Next question

IgM paraproteinaemia - ?Waldenstrom's macroglobulinaemia

This patient has Waldenstrom's macroglobulinaemia. Hyperviscosity syndrome is present in around 10-15% of patients. Other common complications include hepatosplenomegaly.

**Waldenstrom's macroglobulinaemia**

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

**Features**

- monoclonal IgM paraproteinaemia
- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

A 64-year-old woman with metastatic breast cancer is brought in by her husband. Over the past two days she has developed increasingly severe back pain. Her husband reports that her legs are weak and she is having difficulty walking. On examination she has reduced power in both legs and increased tone associated with brisk knee and ankle reflexes. There is some sensory loss in the lower limbs and feet but perianal sensation is normal. What is the most likely diagnosis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Spinal cord compression at T10       |
| <input type="radio"/> | B. Cauda equina syndrome                |
| <input type="radio"/> | C. Guillain Barre syndrome              |
| <input type="radio"/> | D. Hypercalcaemia                       |
| <input type="radio"/> | E. Paraneoplastic peripheral neuropathy |

[Next question](#)

The upper motor neuron signs point towards a diagnosis of spinal cord compression above L1, rather than cauda equina syndrome.

### Spinal cord compression

Spinal cord compression is an oncological emergency and affects up to 5% of cancer patients. Extradural compression accounts for the majority of cases, usually due to vertebral body metastases. It is more common in patients with lung, breast and prostate cancer

#### Features

- back pain - the earliest and most common symptom - may be worse on lying down and coughing
- lower limb weakness
- sensory changes: sensory loss and numbness
- neurological signs depend on the level of the lesion. Lesions above L1 usually result in upper motor neuron signs in the legs and a sensory level. Lesions below L1 usually cause lower motor neuron signs in the legs and perianal numbness. Tendon reflexes tend to be increased below the level of the lesion and absent at the level of the lesion

#### Management

- high-dose oral dexamethasone
- urgent oncological assessment for consideration of radiotherapy or surgery

Which one of the following is least associated with thymomas?

<input type="radio"/>	A. Syndrome inappropriate ADH
<input type="radio"/>	B. Myasthenia gravis
<input type="radio"/>	C. Red cell aplasia
<input type="radio"/>	D. Dermatomyositis
<input type="radio"/>	E. Motor neurone disease

Next question

## Thymoma

Thymomas are the most common tumour of the anterior mediastinum

Associated with

- myasthenia gravis (30-40% of patients with thymoma)
- red cell aplasia
- dermatomyositis
- also : SLE, SIADH

Causes of death

- compression of airway
- cardiac tamponade

A 28-year-old man is investigated for cervical lymphadenopathy. A biopsy shows nodular sclerosing Hodgkin's lymphoma. Which one of the following factors is associated with a poor prognosis?

<input type="radio"/>	A. History of Epstein Barr virus infection
<input type="radio"/>	B. Mediastinal involvement
<input type="radio"/>	C. Female sex
<input type="radio"/>	D. Night sweats
<input type="radio"/>	E. Lymphocytes 20% of total white blood cells

[Next question](#)

Night sweats are a 'B' symptom and imply a poor prognosis

### Hodgkin's lymphoma: histological classification and prognosis

Hodgkin's lymphoma is a malignant proliferation of lymphocytes characterised by the presence of the Reed-Sternberg cell. It has a bimodal age distributions being most common in the third and seventh decades

Histological classification

- nodular sclerosing: most common, good prognosis
- mixed cellularity: good prognosis
- lymphocyte predominant: best prognosis
- lymphocyte depleted: least common, worst prognosis

'B' symptoms also imply a poor prognosis

- weight loss > 10% in last 6 months
- fever > 38°C
- night sweats

Other factors associated with a poor prognosis identified in a 1998 NEJM paper included:

- age > 45 years
- stage IV disease
- haemoglobin < 10.5 g/dl
- lymphocyte count < 600/ $\mu$ l or < 8%
- male
- albumin < 40 g/l
- white blood count > 15,000/ $\mu$ l

A 24-year-old man is diagnosed with a deep vein thrombosis of his right leg. He is initially treated with low-molecular weight heparin but is switched after three days to warfarin. He then develops necrotic skin lesions on his lower limbs and forearms. Which one of the following conditions is characteristically associated with this complication?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Protein S deficiency           |
| <input type="radio"/> | B. Antiphospholipid syndrome      |
| <input type="radio"/> | C. Antithrombin III deficiency    |
| <input type="radio"/> | D. Activated protein C resistance |
| <input type="radio"/> | E. Protein C deficiency           |

[Next question](#)

### Protein C deficiency

Protein C deficiency is an autosomal codominant condition which causes an increased risk of thrombosis

#### Features

- venous thromboembolism
- skin necrosis following the commencement of warfarin: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis



In idiopathic thrombocytopenic purpura what are the autoantibodies most commonly directed at?

<input type="radio"/>	A. Platelet activating factor
<input type="radio"/>	B. Glycoprotein IIb/IIIa complex
<input type="radio"/>	C. ATP receptor
<input type="radio"/>	D. Anti-thrombin III receptor
<input type="radio"/>	E. ADP receptor

Next question

## ITP

Idiopathic thrombocytopenic purpura (ITP) is an immune mediated reduction in the platelet count. Antibodies are directed against the glycoprotein IIb-IIIa or Ib complex.

ITP can be divided into acute and chronic forms:

### Acute ITP

- more commonly seen in children
- equal sex incidence
- may follow an infection or vaccination
- usually runs a self-limiting course over 1-2 weeks

### Chronic ITP

- more common in young/middle-aged women
- tends to run a relapsing-remitting course

### Evan's syndrome

- ITP in association with autoimmune haemolytic anaemia (AIHA)

**Question 107 of 139**

Next

A 67-year-old man is investigated for dyspepsia. A gastroscopy reveals a suspicious lesion which is biopsied. Which one of the following findings on biopsy would be most consistent with a diagnosis of gastric adenocarcinoma?

<input type="radio"/>	A. Columnar metaplasia
<input type="radio"/>	B. Histiocytic infiltration
<input type="radio"/>	C. Paneth cell metaplasia
<input type="radio"/>	D. Giant cell granulomas
<input type="radio"/>	E. Signet ring cells

Next question

Gastric adenocarcinoma - signet ring cells

**Gastric cancer****Epidemiology**

- overall incidence is decreasing, but incidence of tumours arising from the cardia is increasing
- peak age = 70-80 years
- more common in Japan, China, Finland and Colombia than the West
- more common in males, 2:1

**Associations**

- *H. pylori* infection
- blood group A: gAstric cAncer
- gastric adenomatous polyps
- pernicious anaemia
- smoking
- diet: salty, spicy, nitrates
- may be negatively associated with duodenal ulcer

**Investigation**

- diagnosis: endoscopy with biopsy
- staging: CT or endoscopic ultrasound - endoscopic ultrasound has recently been shown to be superior to CT

A 34-year-old man who is known to have type 1 von Willebrand's disease asks for advice. He is due to have a tooth extracted at the dentist next week. Which one of the following is the most appropriate management to reduce the risk of bleeding?

<input type="radio"/>	A. Mefenamic acid
<input type="radio"/>	B. Vitamin K
<input type="radio"/>	C. Desmopressin
<input type="radio"/>	D. Factor VIII concentrate
<input type="radio"/>	E. Factor VII concentrate

[Next question](#)

Blood products such as factor VIII concentrate should be avoided when possible to minimise the risk of transfusion acquired viral illnesses.

### Von Willebrand's disease

Von Willebrand's disease is the most common inherited bleeding disorder. The majority of cases are inherited in an autosomal dominant fashion\* and characteristically behaves like a platelet disorder i.e. epistaxis and menorrhagia are common whilst haemarthroses and muscle haematomas are rare

#### Role of von Willebrand factor

- large glycoprotein which forms massive multimers up to 1,000,000 Da in size
- promotes platelet adhesion to damaged endothelium
- carrier molecule for factor VIII

#### Types

- type 1: partial reduction in vWF (80% of patients)
- type 2: abnormal form of vWF
- type 3: total lack of vWF (autosomal recessive)

#### Investigation

- prolonged bleeding time
- APTT may be prolonged
- factor VIII levels may be moderately reduced
- defective platelet aggregation with ristocetin

#### Management

- tranexamic acid for mild bleeding
- desmopressin (DDAVP): raises levels of vWF by inducing release of vWF from Weibel-Palade bodies in endothelial cells
- factor VIII concentrate

\*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

A 54-year-old woman who has had a hysterectomy presents for advice about hormone replacement therapy. Which one of the following would result from the use of a combined oestrogen-progestogen preparation compared to an oestrogen-only preparation?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Decreased risk of venous thromboembolism |
| <input type="radio"/> | B. Increased risk of a stroke               |
| <input type="radio"/> | C. Increased risk of breast cancer          |
| <input type="radio"/> | D. Increased risk of endometrial cancer     |
| <input type="radio"/> | E. Better control of symptoms               |

[Next question](#)

HRT: adding a progestogen increases the risk of breast cancer

This is the rationale behind giving women who've had a hysterectomy oestrogen-only treatment. The BNF states that the stroke risk is the same regardless of whether the HRT preparation contains progesterone.

### Hormone replacement therapy: adverse effects

Hormone replacement therapy (HRT) involves the use of a small dose of oestrogen (combined with a progestogen in women with a uterus) to help alleviate menopausal symptoms.

#### Side-effects

- nausea
- breast tenderness
- fluid retention and weight gain

#### Potential complications

- increased risk of breast cancer: increased by the addition of a progestogen
- increased risk of endometrial cancer: reduced by the addition of a progestogen but not eliminated completely. The BNF states that the additional risk is eliminated if a progestogen is given continuously
- increased risk of venous thromboembolism: increased by the addition of a progestogen
- increased risk of stroke
- increased risk of ischaemic heart disease if taken more than 10 years after menopause

#### Breast cancer

- in the Women's Health Initiative (WHI) study there was a relative risk of 1.26 at 5 years of developing breast cancer
- the increased risk relates to duration of use
- breast cancer incidence is higher in women using combined preparations compared to oestrogen-only preparations
- the risk of breast cancer begins to decline when HRT is stopped and by 5 years it reaches the same level as in women who have never taken HRT

**Question 110 of 139**

Next

A 66-year-old woman is referred by her GP with anaemia. She has been feeling generally unwell for the past 3 weeks. Bloods on admission show:

Hb	8.7 g/dl
MCV	87 fl
Plt	$198 \times 10^9/l$
WBC	$5.3 \times 10^9/l$

Further tests were then ordered:

Reticulocytes	5.2%
Direct antiglobulin test	Positive, IgG only
Film	Marked red cell agglutination at room temperature

Which one of the following is the most likely underlying cause?

- ☐ A. Non-Hodgkin's lymphoma
- ☐ B. Mycoplasma pneumonia
- ☐ C. Chronic myeloid leukaemia
- ☐ D. Acute myeloid leukaemia subtype M3
- ☐ E. Cytomegalovirus infection

Next question

The blood results suggest warm autoimmune haemolytic anaemia (AIHA) which may be caused by non-Hodgkin's lymphoma. Mycoplasma pneumonia is associated with cold AIHA. The other three listed conditions are not commonly associated with AIHA.

**Autoimmune haemolytic anaemia**

Autoimmune haemolytic anaemia (AIHA) may be divided into 'warm' and 'cold' types, according to at what temperature the antibodies best cause haemolysis. It is most commonly idiopathic but may be secondary to a lymphoproliferative disorder, infection or drugs. AIHA is characterised by a positive direct antiglobulin test (Coombs' test)

**Warm AIHA**

In warm AIHA the antibody (usually IgG) causes haemolysis best at body temperature and haemolysis tends to occur in extravascular sites, for example the spleen. Management options include steroids, immunosuppression and splenectomy

Causes of warm AIHA

- autoimmune disease: e.g. systemic lupus erythematosus\*
- neoplasia: e.g. lymphoma, CLL
- drugs: e.g. methyl dopa

## **Cold AIHA**

The antibody in cold AIHA is usually IgM and causes haemolysis best at 4 deg C. Haemolysis is mediated by complement and is more commonly intravascular. Features may include symptoms of Raynaud's and acrocynaosis. Patients respond less well to steroids

### **Causes of cold AIHA**

- neoplasia: e.g. lymphoma
- infections: e.g. mycoplasma, EBV

\*systemic lupus erythematosus can rarely be associated with a mixed-type autoimmune haemolytic anaemia



Which one of the following is not a risk factor for the development of bladder cancer?

<input type="radio"/>	A. Occupational exposure to aniline dyes
<input type="radio"/>	B. Cyclophosphamide
<input type="radio"/>	C. Strongyloides infection
<input type="radio"/>	D. Smoking
<input type="radio"/>	E. Occupational history involving rubber manufacture

Next question

Schistosomiasis rather than Strongyloides infection is associated with an increased risk of bladder cancer

### Bladder cancer: risk factors

The following factors are associated with the development of bladder cancer:

- smoking
- occupational: aniline dyes used in printing and textile industry, rubber manufacture
- schistosomiasis
- drugs: cyclophosphamide

**Question 112 of 139**

Next

A 17-year-old man is investigated after he bled excessively following a tooth extraction. The following results are obtained:

Plt	173 * 10 <sup>9</sup> /l
PT	12.9 secs
APTT	84 secs

Which clotting factor is he most likely to be deficient in?

- ☐ A. Factor VI
- ☐ B. Factor VII
- ☒ C. Factor VIII
- ☐ D. Factor IX
- ☐ E. Factor X

Next question

This man is most likely to have haemophilia A, which accounts for 90% of cases of haemophilia.

**Haemophilia**

Haemophilia is a X-linked recessive disorder of coagulation. Up to 30% of patients have no family history of the condition. Haemophilia A is due to a deficiency of factor VIII whilst in haemophilia B (Christmas disease) there is a lack of factor IX

**Features**

- haemarthroses, haematomas
- prolonged bleeding after surgery or trauma

**Blood tests**

- prolonged APTT
- bleeding time, thrombin time, prothrombin time normal

Up to 10-15% of patients with haemophilia A develop antibodies to factor VIII treatment

A 48-year-old female who has just completed a course of chemotherapy complains of difficulty using her hands associated with 'pins and needles'. She has also experienced urinary hesitancy. Which cytotoxic drug is most likely to be responsible?

- ☐ A. Doxorubicin
- ☐ B. Cyclophosphamide
- ☐ C. Methotrexate
- ☒ D. Vincristine
- ☐ E. Bleomycin

Vincristine - peripheral neuropathy

Vincristine is associated with peripheral neuropathy. Urinary hesitancy may develop secondary to bladder atony.

### Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

### Question 114 of 139

A 67-year-old woman is diagnosed with multiple myeloma. Which one of the following complications is she most likely to develop as a result of her primary diagnosis?

<input type="radio"/>	A. Renal failure
<input type="radio"/>	B. Venous thromboembolism
<input type="radio"/>	C. Hypercalcaemia
<input type="radio"/>	D. Carpal tunnel syndrome
<input type="radio"/>	E. Pathological fracture

[Next question](#)

This is a difficult question as all of the above may be seen with myeloma. However, up to 60% of patients will develop a pathological fracture.

#### Myeloma: features

Multiple myeloma is a neoplasm of the bone marrow plasma cells. The peak incidence is patients aged 60-70 years.

##### Clinical features

- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

##### Diagnosis is based on:

- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

##### Hypercalcaemia in myeloma

- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

Which electrolyte disturbance is cisplatin most associated with?

- ☐ A. Hypocalcaemia
- ☐ B. Hyponatraemia
- ☐ C. Hypomagnesaemia
- ☐ D. Hypokalaemia
- ☐ E. Hypercalcaemia

Next question

Cisplatin is associated with hypomagnesaemia

### Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia

Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis
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## Question 116 of 139

Of the following options, which one is the best diagnostic test for paroxysmal nocturnal haemoglobinuria?

<input type="radio"/>	A. Osmotic fragility test
<input type="radio"/>	B. FMC-7 staining
<input type="radio"/>	C. PAS staining of erythrocytes
<input type="radio"/>	D. Flow cytometry for CD59 and CD55
<input type="radio"/>	E. Immunophenotyping for CD19 and CD20

Next question

Flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in paroxysmal nocturnal haemoglobinuria

### Paroxysmal nocturnal haemoglobinuria

Paroxysmal nocturnal haemoglobinuria (PNH) is an acquired disorder leading to haemolysis (mainly intravascular) of haematological cells. It is thought to be caused by increased sensitivity of cell membranes to complement (see below) due to a lack of glycoprotein glycosyl-phosphatidylinositol (GPI). Patients are more prone to venous thrombosis

#### Pathophysiology

- GPI can be thought of as an anchor which attaches surface proteins to the cell membrane
- complement-regulating surface proteins, e.g. decay-accelerating factor (DAF), are not properly bound to the cell membrane due a lack of GPI
- thrombosis is thought to be caused by a lack of CD59 on platelet membranes predisposing to platelet aggregation

#### Features

- haemolytic anaemia
- red blood cells, white blood cells, platelets or stem cells may be affected therefore pancytopenia may be present
- haemoglobinuria: classically dark-coloured urine in the morning (although has been shown to occur throughout the day)
- thrombosis e.g. Budd-Chiari syndrome
- aplastic anaemia may develop in some patients

#### Diagnosis

- flow cytometry of blood to detect low levels of CD59 and CD55 has now replaced Ham's test as the gold standard investigation in PNH
- Ham's test: acid-induced haemolysis (normal red cells would not)

## Management

- blood product replacement
- anticoagulation
- eculizumab, a monoclonal antibody directed against terminal protein C5, is currently being trialled and is showing promise in reducing intravascular haemolysis
- stem cell transplantation



### Question 117 of 139

A 25-year-old woman with primary antiphospholipid syndrome is reviewed. She has just had a booking ultrasound at 11 weeks gestation which confirms a viable pregnancy. This is her first pregnancy and she is otherwise fit and well. Which one of the following is the recommend treatment?

- |                                  |  |
|----------------------------------|--|
| <input type="radio"/>            | A. Aspirin + prednisolone                      |
| <input type="radio"/>            | B. Low-molecular weight heparin                |
| <input type="radio"/>            | C. Prednisolone + low-molecular weight heparin |
| <input checked="" type="radio"/> | D. Aspirin + low-molecular weight heparin      |
| <input type="radio"/>            | E. Aspirin                                     |

[Next question](#)

Antiphospholipid syndrome in pregnancy: aspirin + LMWH

The ultrasound at 11 weeks gestation would show a fetal heart if the pregnancy was viable. This patient should therefore be taking both aspirin and low-molecular weight heparin.

#### Antiphospholipid syndrome: pregnancy

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

In pregnancy the following complications may occur:

- recurrent miscarriage
- IUGR
- pre-eclampsia
- placental abruption
- pre-term delivery
- venous thromboembolism

#### Management

- low-dose aspirin should be commenced once the pregnancy is confirmed on urine testing
- low molecular weight heparin once a fetal heart is seen on ultrasound. This is usually discontinued at 34 weeks gestation
- these interventions increase the live birth rate seven-fold

A 61-year-old woman is investigated for hoarseness and dyspnoea which has got progressively worse over the past month. In the past she has been diagnosed with toxic multinodular goitre which was successfully treated with radioiodine. On examination she has a firm, asymmetrical swelling of the thyroid gland. Laryngoscopy demonstrates a right vocal cord paralysis and apparent external compression of the trachea. What is the most likely diagnosis?

- ☐ A. Follicular thyroid cancer
- ☐ B. Papillary thyroid cancer
- ☐ C. Medullary thyroid cancer
- ☐ D. Lymphoma of the thyroid gland
- ☐ E. Anaplastic thyroid cancer

Next question

Anaplastic thyroid cancer - aggressive, difficult to treat and often causes pressure symptoms

### Thyroid cancer

Features of hyperthyroidism or hypothyroidism are not commonly seen in patients with thyroid malignancies as they rarely secrete thyroid hormones

Type	Percentage	
Papillary	70%	Often young females - excellent prognosis
Follicular	20%	
Medullary	5%	Cancer of parafollicular cells, secrete calcitonin, part of MEN-2
Anaplastic	1%	Not responsive to treatment, can cause pressure symptoms
Lymphoma	Rare	Associated with Hashimoto's

Management of papillary and follicular cancer

- total thyroidectomy
- followed by radioiodine (I-131) to kill residual cells
- yearly thyroglobulin levels to detect early recurrent disease

A 48-year-old man is diagnosed with acute myeloid leukaemia and cytogenetics are performed. Which one of the following is associated most with a poor prognosis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Deletions of chromosome 5                  |
| <input type="radio"/> | B. Translocation between chromosome 15 and 17 |
| <input type="radio"/> | C. Deletions of chromosome 15                 |
| <input type="radio"/> | D. Translocation between chromosome 9 and 14  |
| <input type="radio"/> | E. Deletions of chromosome 8                  |

[Next question](#)

Acute myeloid leukaemia - poor prognosis: deletion of chromosome 5 or 7

### Acute myeloid leukaemia

Acute myeloid leukaemia is the more common form of acute leukaemia in adults. It may occur as a primary disease or following a secondary transformation of a myeloproliferative disorder.

Poor prognostic features

- > 60 years
- > 20% blasts after first course of chemo
- cytogenetics: deletions of chromosome 5 or 7

Acute promyelocytic leukaemia M3

- associated with t(15;17)
- fusion of PML and RAR-alpha genes
- presents younger than other types of AML (average = 25 years old)
- DIC or thrombocytopenia often at presentation
- good prognosis

Classification - French-American-British (FAB)

- M0 - undifferentiated
- M1 - without maturation
- M2 - with granulocytic maturation
- M3 - acute promyelocytic

- M4 - granulocytic and monocytic maturation
- M5 - monocytic
- M6 - erythroleukaemia
- M7 - megakaryoblastic

A 52-year-old is found to have chronic myeloid leukaemia following investigation for splenomegaly. Which one of the following best describes the function of the BCR-ABL fusion protein?

<input type="radio"/>	A. Epidermal growth factor receptor
<input type="radio"/>	B. Phospholipase C
<input type="radio"/>	C. CD52 co-receptor
<input type="radio"/>	D. Tyrosine kinase
<input type="radio"/>	E. Fibroblast growth factor receptor

[Next question](#)

Chronic myeloid leukaemia - imatinib = tyrosine kinase inhibitor

### Chronic myeloid leukaemia

The Philadelphia chromosome is present in more than 95% of patients with chronic myeloid leukaemia (CML). It is due to a translocation between the long arm of chromosome 9 and 22 - t(9:22)(q34; q11). This results in part of the ABL proto-oncogene from chromosome 9 being fused with the BCR gene from chromosome 22. The resulting BCR-ABL gene codes for a fusion protein which has tyrosine kinase activity in excess of normal

Presentation (40-50 years)

- middle-age
- anaemia, weight loss, abdo discomfort
- splenomegaly may be marked
- spectrum of myeloid cells seen in peripheral blood
- decreased neutrophil alkaline phosphatase
- may undergo blast transformation (AML in 80%, ALL in 20%)

Management

- imatinib is now considered first-line treatment
- hydroxyurea
- interferon-alpha
- allogenic bone marrow transplant

Imatinib

- inhibitor of the tyrosine kinase associated with the BCR-ABL defect
- very high response rate in chronic phase CML

Transmission of which type of infection is most likely to occur following a platelet transfusion?

<input type="radio"/>	A. Syphilis
<input type="radio"/>	B. Malaria
<input type="radio"/>	C. Hepatitis B
<input checked="" type="radio"/>	D. Bacterial
<input type="radio"/>	E. HIV

Next question

As platelet concentrates are generally stored at room temperature they provide a more favourable environment for bacterial contamination than other blood products.

### Blood product transfusion complications

#### Complications

- haemolytic: immediate or delayed
- febrile reactions
- transmission of viruses, bacteria, parasites
- hyperkalaemia
- iron overload
- ARDS
- clotting abnormalities

#### Immediate haemolytic reaction

- e.g. ABO mismatch
- massive intravascular haemolysis

#### Febrile reactions

- due to white blood cell HLA antibodies
- often the result of sensitization by previous pregnancies or transfusions

#### Causes a degree of immunosuppression

- e.g. patients with colorectal cancer who have blood transfusions have a worse outcome than those who do not

Patients with Sjogren's syndrome are at an increased risk of which one of the following malignancies?

<input type="radio"/>	A. Myeloma
<input type="radio"/>	B. Oesophageal cancer
<input type="radio"/>	C. Intraocular melanoma
<input type="radio"/>	D. Squamous cell skin cancer
<input type="radio"/>	E. Non-Hodgkin's lymphoma

Patients with Sjogren's syndrome have an increased risk of lymphoid malignancies

### Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

#### Features

- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

#### Investigation

- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

#### Management

- artificial saliva and tears
- pilocarpine may stimulate saliva production

A 77-year-old man with a history of chronic lymphocytic leukaemia is admitted to the Acute Medical Unit with pneumonia. This is his fourth admission for pneumonia in the past six months. Which one of the following factors is most likely to be responsible?

<input type="radio"/>	A. Hypersplenism
<input type="radio"/>	B. Decreased lymphocyte survival
<input type="radio"/>	C. Hypogammaglobulinaemia
<input type="radio"/>	D. Transformation to high-grade lymphoma
<input type="radio"/>	E. Immature lymphocytes

[Next question](#)

### Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

#### Features

- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

#### Complications

- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

#### Investigations

- blood film: smudge cells
- immunophenotyping



Burkitt's lymphoma is associated with which one of the following genetic changes:

- |                                  |                                     |
|----------------------------------|-------------------------------------|
| <input type="radio"/>            | A. Cyclin D1-IGH gene translocation |
| <input type="radio"/>            | B. TEL-JAK2 gene translocation      |
| <input type="radio"/>            | C. Bcl-2 gene translocation         |
| <input checked="" type="radio"/> | D. C-myc gene translocation         |
| <input type="radio"/>            | E. BCR-Abl1 gene translocation      |

Next question

Burkitt's lymphoma - c-myc gene translocation

### Burkitt's lymphoma

Burkitt's lymphoma is a high-grade B-cell neoplasm. There are two major forms:

- endemic (African) form: typically involves maxilla or mandible
- sporadic form: abdominal (e.g. ileo-caecal) tumours are the most common form. More common in patients with HIV

Burkitt's lymphoma is associated with the c-myc gene translocation, usually t(8:14). The Epstein-Barr virus (EBV) is strongly implicated in the development of the African form of Burkitt's lymphoma and to a lesser extent the sporadic form.

Management is with chemotherapy. This tends to produce a rapid response which may cause 'tumour lysis syndrome'. Complications of tumour lysis syndrome include:

- hyperkalaemia
- hyperphosphataemia
- hypocalcaemia
- hyperuricaemia
- acute renal failure

A 34-year-old man is reviewed four years after having an orchidectomy for a testicular teratoma. What are the most useful follow-up investigation(s) to detect disease recurrence?

- ☐ A. CRP + beta-HCG
- ☐ B. Testosterone + beta-HCG
- ☐ C. ESR + alpha-fetoprotein
- ☐ D. Alpha-fetoprotein + beta-HCG
- ☐ E. LDH + ESR

### Tumour markers

Tumour markers may be divided into:

- monoclonal antibodies against carbohydrate or glycoprotein tumour antigens
- tumour antigens
- enzymes (alkaline phosphatase, neurone specific enolase)
- hormones (e.g. calcitonin, ADH)

It should be noted that tumour markers usually have a low specificity

### Monoclonal antibodies

Tumour marker	Association
CA 125	Ovarian cancer
CA 19-9	Pancreatic cancer
CA 15-3	Breast cancer

### Tumour antigens

Tumour marker	Association
Prostate specific antigen (PSA)	Prostatic carcinoma
Alpha-feto protein (AFP)	Hepatocellular carcinoma, teratoma
Carcinoembryonic antigen (CEA)	Colorectal cancer

**Question 126 of 139**

Next

A 71-year-old woman with no significant past medical history is investigated for lymphocytosis. She has recently lost 7kg in weight and complains of lethargy. The following blood results are obtained:

Hb	9.8 g/dl
Plt	$104 \times 10^9/l$
WBC	$70.3 \times 10^9/l$
Blood film:	Lymphocytosis. Smudge cells seen

Four months previously her white cell count was  $30.5 \times 10^9/l$ . What is the most appropriate management?

- ☐ A. Imatinib
- ☐ B. Chlorambucil
- ☐ C. No treatment, monitor full blood count
- ☐ D. Fludarabine, cyclophosphamide and rituximab
- ☐ E. Allogeneic stem cell transplantation

Next question

CLL - treatment: Fludarabine, Cyclophosphamide and Rituximab (FCR)

This patient has chronic lymphocytic leukaemia. The lymphocyte doubling time is less than 6 months, the patient has some evidence of marrow failure and also has systemic symptoms. She should therefore be treated and of the options given a combination of fludarabine, cyclophosphamide and rituximab (FCR) is the most appropriate treatment. Chlorambucil used to be the first-line treatment of choice but studies have shown it not to be as effective as FCR.

As with many haematological cancers such patients are often entered into randomised trials

**Chronic lymphocytic leukaemia: management****Indications for treatment**

- progressive marrow failure: the development or worsening of anaemia and/or thrombocytopenia
- massive ( $>10$  cm) or progressive lymphadenopathy
- massive ( $>6$  cm) or progressive splenomegaly
- progressive lymphocytosis:  $> 50\%$  increase over 2 months or lymphocyte doubling time  $< 6$  months
- systemic symptoms: weight loss  $> 10\%$  in previous 6 months, fever  $>38^\circ\text{C}$  for  $> 2$  weeks, extreme fatigue, night sweats
- autoimmune cytopenias e.g. ITP

## Management

- patients who have no indications for treatment are monitored with regular blood counts
- fludarabine, cyclophosphamide and rituximab (FCR) has now emerged as the initial treatment of choice for the majority of patients

What is the lifetime risk of developing colorectal cancer in the United Kingdom?

- |                       |        |
|-----------------------|--------|
| <input type="radio"/> | A. 1%  |
| <input type="radio"/> | B. 2%  |
| <input type="radio"/> | C. 5%  |
| <input type="radio"/> | D. 10% |
| <input type="radio"/> | E. 15% |

Next question

Colorectal cancer is the third most common cancer in the UK, with approximately 30,000 new cases in England and Wales per year

### Colorectal cancer: screening

#### Overview

- most cancers develop from adenomatous polyps. Screening for colorectal cancer has been shown to reduce mortality by 16%
- the NHS now has a national screening programme offering screening every 2 years to all men and women aged 60 to 69 years. Patients aged over 70 years may request screening
- eligible patients are sent faecal occult blood (FOB) tests through the post
- patients with abnormal results are offered a colonoscopy

At colonoscopy, approximately:

- 5 out of 10 patients will have a normal exam
- 4 out of 10 patients will be found to have polyps which may be removed due to their premalignant potential
- 1 out of 10 patients will be found to have cancer

Which one of the following is the most common inherited thrombophilia?

- |                                  |                                   |
|----------------------------------|-----------------------------------|
| <input type="radio"/>            | A. Protein S deficiency           |
| <input type="radio"/>            | B. Antithrombin III deficiency    |
| <input type="radio"/>            | C. Protein C deficiency           |
| <input checked="" type="radio"/> | D. Activated protein C resistance |
| <input type="radio"/>            | E. Von Willebrand's disease       |

Next question

Activated protein C resistance (Factor V Leiden) is the most common inherited thrombophilia

Activated protein C resistance is due a point mutation in the Factor V gene, encoding for the Leiden allele. Heterozygotes have a 5-fold risk of venous thrombosis whilst homozygotes have a 50-fold increased risk

Von Willebrand's disease is the most common inherited bleeding disorder

### Thrombophilia: causes

#### Inherited

- activated protein C resistance (factor V Leiden)
- antithrombin III deficiency
- protein C deficiency
- protein S deficiency

#### Acquired

- antiphospholipid syndrome
- the Pill

Each one of the following is associated with polycythaemia rubra vera, except:

<input type="radio"/>	A. Splenomegaly
<input type="radio"/>	B. Hyperviscosity
<input type="radio"/>	C. Raised ESR
<input type="radio"/>	D. Hypertension
<input type="radio"/>	E. Pruritus

Next question

Polycythaemia rubra vera is associated with a low ESR

### Polycythaemia rubra vera: features

Polycythaemia rubra vera (PRV) is a myeloproliferative disorder caused by clonal proliferation of a marrow stem cell leading to an increase in red cell volume, often accompanied by overproduction of neutrophils and platelets. It has recently been established that a mutation in JAK2 is present in approximately 95% of patients with PRV and this has resulted in significant changes to the diagnostic criteria. The incidence of PRV peaks in the sixth decade.

#### Features

- hyperviscosity
- pruritus, typically after a hot bath
- splenomegaly
- haemorrhage (secondary to abnormal platelet function)
- plethoric appearance
- hypertension in a third of patients

Following history and examination, the British Committee for Standards in Haematology (BCSH) recommend the following tests are performed

- full blood count/film (raised haematocrit; neutrophils, basophils, platelets raised in half of patients)
- JAK2 mutation
- serum ferritin
- renal and liver function tests

If the JAK2 mutation is negative and there is no obvious secondary causes the BCSH suggest the following tests:

- red cell mass
- arterial oxygen saturation
- abdominal ultrasound
- serum erythropoietin level
- bone marrow aspirate and trephine
- cytogenetic analysis
- erythroid burst-forming unit (BFU-E) culture

Other features that may be seen in PRV include a low ESR and a raised leukocyte alkaline phosphatase

The diagnostic criteria for PRV have recently been updated by the BCSH. This replaces the previous PRV Study Group criteria.

JAK2-positive PRV - diagnosis requires both criteria to be present

A1	High haematocrit (>0.52 in men, >0.48 in women) OR raised red cell mass (>25% above predicted)
A2	Mutation in JAK2

JAK2-negative PRV - diagnosis requires A1 + A2 + A3 + either another A or two B criteria

A1	Raised red cell mass (>25% above predicted) OR haematocrit >0.60 in men, >0.56 in women
A2	Absence of mutation in JAK2
A3	No cause of secondary erythrocytosis
A4	Palpable splenomegaly
A5	Presence of an acquired genetic abnormality (excluding BCR-ABL) in the haematopoietic cells
B1	Thrombocytosis (platelet count $>450 \times 10^9/l$ )
B2	Neutrophil leucocytosis (neutrophil count $> 10 \times 10^9/l$ in non-smokers; $> 12.5 \times 10^9/l$ in smokers)
B3	Radiological evidence of splenomegaly
B4	Endogenous erythroid colonies or low serum erythropoietin



A 4-year-old girl with sickle cell anaemia presents with abdominal pain. On examination she is noted to have splenomegaly and is clinically anaemic. What is the most likely diagnosis?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. Liver cirrhosis             |
| <input type="radio"/> | B. Parvovirus infection        |
| <input type="radio"/> | C. Sequestration crisis        |
| <input type="radio"/> | D. <i>Salmonella</i> infection |
| <input type="radio"/> | E. Thrombotic crisis           |

### Sickle-cell crises

Sickle cell anaemia is characterised by periods of good health with intervening crises

Four main types of crises are recognised:

- thrombotic, 'painful crises'
- sequestration
- aplastic
- haemolytic

#### Thrombotic crises

- also known as painful crises or vaso-occlusive crises
- precipitated by infection, dehydration, deoxygenation
- infarcts occur in various organs including the bones (e.g. avascular necrosis of hip, hand-foot syndrome in children, lungs, spleen and brain)

#### Sequestration crises

- sickling within organs such as the spleen or lungs causes pooling of blood with worsening of the anaemia
- acute chest syndrome: dyspnoea, chest pain, pulmonary infiltrates, low pO<sub>2</sub> - the most common cause of death after childhood

#### Aplastic crises

- caused by infection with parvovirus
- sudden fall in haemoglobin

#### Haemolytic crises

- rare
- fall in haemoglobin due to an increased rate of haemolysis

Which one of the following statements regarding heparin-induced thrombocytopenia (HIT) is correct?

- ☐ A. A fall in the platelet count of greater than 15% is diagnostic
- ☐ B. HIT is a prothrombotic condition
- ☐ C. Tranexamic acid is the treatment of choice
- ☐ D. HIT usually develops with 2-3 days of starting treatment
- ☐ E. HIT is more common with low-molecular weight heparin than with unfractionated heparin

[Next question](#)

## Heparin

There are two main types of heparin - unfractionated, 'standard' heparin or low molecular weight heparin (LMWH). Heparins generally act by activating antithrombin III. Unfractionated heparin forms a complex which inhibits thrombin, factors Xa, IXa, XIa and XIIa. LMWH however only increases the action of antithrombin III on factor Xa

The table below shows the differences between standard heparin and LMWH:

	Standard heparin	Low molecular weight heparin (LMWH)
<b>Administration</b>	Intravenous	Subcutaneous
<b>Duration of action</b>	Short	Long
<b>Mechanism of action</b>	Activates antithrombin III. Forms a complex that inhibits thrombin, factors Xa, IXa, XIa and XIIa	Activates antithrombin III. Forms a complex that inhibits factor Xa
<b>Side-effects</b>	Bleeding Heparin-induced thrombocytopenia (HIT) Osteoporosis	Bleeding  Lower risk of HIT and osteoporosis with LMWH
<b>Monitoring</b>	Activated partial thromboplastin time (APTT)	Anti-Factor Xa (although routine monitoring is not required)
<b>Notes</b>	Useful in situations where there is a high risk of bleeding as anticoagulation can be terminated rapidly	Now standard in the management of venous thromboembolism treatment and prophylaxis and acute coronary syndromes

## Heparin-induced thrombocytopenia (HIT)

- immune mediated - antibodies form which cause the activation of platelets
- usually does not develop until after 5-10 days of treatment
- despite being associated with low platelets HIT is actually a prothrombotic condition
- features include a greater than 50% reduction in platelets, thrombosis and skin allergy
- treatment options include alternative anticoagulants such as lepirudin and danaparoid

Both unfractionated and low-molecular weight heparin can cause hyperkalaemia. This is thought to be caused by inhibition of aldosterone secretion.

Heparin overdose may be reversed by protamine sulphate, although this only partially reverses the effect of LMWH.

Which one of the following features is least associated with Waldenstrom's macroglobulinaemia?

<input type="radio"/>	A. Cryoglobulinaemia
<input type="radio"/>	B. Bone pain
<input type="radio"/>	C. Retinal vein thrombosis
<input type="radio"/>	D. Hepatosplenomegaly
<input type="radio"/>	E. Monoclonal IgM paraproteinaemia

Next question

### Waldenstrom's macroglobulinaemia

Waldenstrom's macroglobulinaemia is an uncommon condition seen in older men. It is a lymphoplasmacytoid malignancy characterised by the secretion of a monoclonal IgM paraprotein

#### Features

- monoclonal IgM paraproteinaemia
- systemic upset: weight loss, lethargy
- hyperviscosity syndrome e.g. visual disturbance
- hepatosplenomegaly
- lymphadenopathy
- cryoglobulinaemia e.g. Raynaud's

Interferon alpha is a recognised treatment for which one of the following haematological disorders?

<input type="radio"/>	A. Acute lymphoblastic leukaemia
<input type="radio"/>	B. Myelofibrosis
<input type="radio"/>	C. Burkitt's lymphoma
<input type="radio"/>	D. Hairy cell leukaemia
<input type="radio"/>	E. Acute myeloid leukaemia

Next question

Interferons (IFN) are cytokines released by the body in response to viral infections and neoplasia. They are classified according to cellular origin and the type of receptor they bind to. IFN-alpha and IFN-beta bind to type 1 receptors whilst IFN-gamma binds only to type 2 receptors.

IFN-alpha is produced by leucocytes and has an antiviral action. It has been shown to be useful in the management of hepatitis B & C, Kaposi's sarcoma, metastatic renal cell cancer and hairy cell leukaemia

### Hairy cell leukaemia

Hairy cell leukaemia is a rare malignant proliferation disorder of B cells. It is more common in males (4:1)

#### Features

- pancytopenia
- splenomegaly
- skin vasculitis in 1/3 patients
- 'dry tap' despite bone marrow hypercellularity
- tartrate resistant acid phosphatase (TRAP) stain positive

#### Management

- chemotherapy is first-line: cladribine, pentostatin
- immunotherapy is second-line: rituximab, interferon-alpha

**Question 134 of 139**

Next

A 17-year-old male is diagnosed with alpha-thalassaemia. What chromosome is the alpha-globulin genes located on?

<input type="radio"/>	A. Chromosome 4
<input type="radio"/>	B. Chromosome 8
<input type="radio"/>	C. Chromosome 12
<input type="radio"/>	D. Chromosome 16
<input type="radio"/>	E. Chromosome 20

Next question

**Alpha-thalassaemia**

Alpha-thalassaemia is due to a deficiency of alpha chains in haemoglobin

**Overview**

- 2 separate alpha-globulin genes are located on each chromosome 16

Clinical severity depends on the number of alpha chains present

If 1 or 2 alpha chains are absent then the blood picture would be hypochromic and microcytic, but the Hb level would be typically normal

Loss of 3 alpha chains results in a hypochromic microcytic anaemia with splenomegaly. This is known as Hb H disease

If all 4 alpha chains absent (i.e. homozygote) then death in utero (hydrops fetalis, Bart's hydrops)

A woman who is about to commence trastuzumab treatment for breast cancer has an echocardiogram. Which class of chemotherapeutic agent would predispose her to developing cardiac dysfunction?

<input type="radio"/>	A. Vinca alkaloids
<input type="radio"/>	B. Platinum-based compounds
<input type="radio"/>	C. Anthracyclines
<input type="radio"/>	D. Taxanes
<input type="radio"/>	E. Topoisomerase I inhibitors

[Next question](#)

### Trastuzumab

Trastuzumab (Herceptin) is a monoclonal antibody directed against the HER2/neu receptor. It is used mainly in metastatic breast cancer although some patients with early disease are now also given trastuzumab.

#### Adverse effects

- flu-like symptoms and diarrhoea are common
- cardiotoxicity: more common when anthracyclines have also been used. An echo is usually performed before starting treatment

Which one of the following is associated with a high leucocyte alkaline phosphatase score?

<input type="radio"/>	A. Myelofibrosis
<input type="radio"/>	B. Pernicious anaemia
<input type="radio"/>	C. Infectious mononucleosis
<input type="radio"/>	D. Paroxysmal nocturnal haemoglobinuria
<input type="radio"/>	E. Chronic myeloid leukaemia

Next question

### Leucocyte alkaline phosphatase

Raised in

- myelofibrosis
- leukaemoid reactions
- polycythaemia rubra vera
- infections
- steroids, Cushing's syndrome
- pregnancy, oral contraceptive pill

Low in

- chronic myeloid leukaemia
- pernicious anaemia
- paroxysmal nocturnal haemoglobinuria
- infectious mononucleosis



A 72-year-old woman is admitted with confusion and pallor. Her daughter reports that she has been getting more confused and tired for the past three months. Blood tests are reported as follows:

Hb	8.9 g/dl
MCV	125 fl
Plt	$148 \times 10^9/l$
WBC	$4.4 \times 10^9/l$

In light of the macrocytic anaemia some further tests are ordered:

Intrinsic factor antibodies	Negative
Vitamin B12	94 ng/l (200-900 ng/l)
Folic acid	1.1 nmol/l (> 3.0 nmol/l)

What is the most appropriate management?

- ☐ A. Oral folic acid + blood transfusion
- ☐ B. Oral folic acid + start Intramuscular vitamin B12 when folic acid levels are normal
- ☐ C. Intramuscular vitamin B12 + start oral folic acid when vitamin B12 levels are normal
- ☐ D. Blood transfusion
- ☐ E. Oral prednisolone

It is important in a patient who is also deficient in both vitamin B12 and folic acid to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord

### Macrocytic anaemia

Macrocytic anaemia can be divided into causes associated with a megaloblastic bone marrow and those with a normoblastic bone marrow

Megaloblastic causes	Normoblastic causes
<ul style="list-style-type: none"> <li>• vitamin B12 deficiency</li> <li>• folate deficiency</li> <li>• cytotoxics e.g. hydroxyurea</li> </ul>	<ul style="list-style-type: none"> <li>• alcohol</li> <li>• liver disease</li> <li>• hypothyroidism</li> <li>• pregnancy</li> <li>• reticulocytosis e.g. haemolysis</li> <li>• aplastic anaemia</li> <li>• myelodysplasia</li> <li>• drugs: cytotoxics</li> </ul>

### Question 138 of 139

Which one of the following statements regarding warfarin is correct?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Warfarin can be used when breast-feeding                                   |
| <input type="radio"/> | B. Hypothyroidism may develop in a small minority of patients                 |
| <input type="radio"/> | C. Aortic prosthetic valves generally require a higher INR than mitral valves |
| <input type="radio"/> | D. The target INR following a pulmonary embolism is 3.5                       |
| <input type="radio"/> | E. All patients with an INR of greater than 6.0 should be given vitamin K     |

[Next question](#)

## Warfarin

Warfarin is an oral anticoagulant which inhibits the reduction of vitamin K to its active hydroquinone form, which in turn acts as a cofactor in the formation of clotting factor II, VII, IX and X (mnemonic = 1972) and protein C .

### Indications

- venous thromboembolism: target INR = 2.5, if recurrent 3.5
- atrial fibrillation, target INR = 2.5
- mechanical heart valves, target INR depends on the valve type and location. Mitral valves generally require a higher INR than aortic valves.

Patients on warfarin are monitored using the INR (international normalised ration), the ratio of the prothrombin time for the patient over the normal prothrombin time. Warfarin has a long half-life and achieving a stable INR may take several days. There a variety of loading regimes and computer software is now often used to alter the dose.

### Factors that may potentiate warfarin

- liver disease
- P450 enzyme inhibitors, e.g.: amiodarone, ciprofloxacin
- cranberry juice
- drugs which displace warfarin from plasma albumin, e.g. NSAIDs
- inhibit platelet function: NSAIDs

### Side-effects

- haemorrhage

- teratogenic, although can be used in breast-feeding mothers
- skin necrosis: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis
- purple toes

### Question 139 of 139

A 71-year-old woman with metastatic breast cancer comes to surgery with her husband. She is known to have spinal metastases but her back pain is not controlled with a combination of paracetamol, diclofenac and MST 30mg bd. Her husband reports she is using 10mg of oral morphine solution around 6-7 times a day for breakthrough pain. The palliative care team at the hospice tried using a bisphosphonate but this unfortunately resulted in persistent myalgia and arthralgia. What is the most appropriate next step?

- A. Switch to oxycodone
- B. Increase MST
- C. Increase MST + add dexamethasone
- D. Increase MST + suggest course of complimentary therapies
- E. Increase MST + refer for radiotherapy

Metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

### Palliative care prescribing: pain

#### NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

#### Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered

#### SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

## Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

## Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

## Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted. NICE give the following advice on conversion:

- a transdermal fentanyl 12 microgram patch equates to approximately 45 mg oral morphine daily
- a transdermal buprenorphine 20 microgram patch equates to approximately 30 mg oral morphine daily.

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Reactive arthritis is associated with which one of the following HLA antigens?

- ☐ A. HLA-B27
- ☐ B. HLA-A3
- ☐ C. HLA-DR4
- ☐ D. HLA-B5
- ☐ E. HLA-DR3

Next question

## Reactive arthritis

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA).

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint.

### Epidemiology

- post-STI form much more common in men (e.g. 10:1)
- post-dysenteric form equal sex incidence

The table below shows the organisms that are most commonly associated with reactive arthritis:

Post-dysenteric form	Post-STI form
<i>Shigella flexneri</i> <i>Salmonella typhimurium</i> <i>Salmonella enteritidis</i> <i>Yersinia enterocolitica</i> <i>Campylobacter</i>	<i>Chlamydia trachomatis</i>

### Management

- symptomatic: analgesia, NSAIDs, intra-articular steroids
- sulfasalazine and methotrexate are sometimes used for persistent disease
- symptoms rarely last more than 12 months

**Question 2 of 118**

Next

A 47-year-old man with a history of chronic sinusitis presents with shortness of breath to the Emergency Department. Initial investigations reveal:

Hb	10.4g/dl
Platelets	$477 \times 10^9/l$
WCC	$14.3 \times 10^9/l$
ESR	92 mm/h
Urea	20 mmol/l
Creatinine	198 $\mu\text{mol/l}$
Urine dipstick	blood + + +

What is the most likely diagnosis?

- ☐ A. Mixed cryoglobulinaemia
- ☐ B. Churg-Strauss syndrome
- ☐ C. Wegener's granulomatosis
- ☐ D. Haemolytic uraemic syndrome
- ☐ E. Henoch-Schonlein purpura

Next question

The combination of pulmonary and renal involvement combined with a history of chronic sinusitis points towards a diagnosis of Wegener's granulomatosis.

**Wegener's granulomatosis**

Wegener's granulomatosis is an autoimmune condition associated with a necrotizing granulomatous vasculitis, affecting both the upper and lower respiratory tract as well as the kidneys

**Features**

- upper respiratory tract: epistaxis, sinusitis, nasal crusting
- lower respiratory tract: dyspnoea, haemoptysis
- glomerulonephritis ('pauci-immune', 80% of patients)
- saddle-shape nose deformity
- also: vasculitic rash, eye involvement (e.g. proptosis), cranial nerve lesions

## Investigations

- cANCA positive in > 90%, pANCA positive in 25%
- chest x-ray: wide variety of presentations, including cavitating lesions
- renal biopsy: crescentic glomerulonephritis

## Management

- steroids
- cyclophosphamide (90% response)
- plasma exchange
- median survival = 8-9 years



### Question 3 of 118

Next

A 50-year-old female with a history of rheumatoid presents with a suspected septic knee joint. A diagnostic aspiration is performed and sent to microbiology. Which of the following organisms is most likely to be responsible?

<input type="radio"/>	A. <i>Staphylococcus aureus</i>
<input type="radio"/>	B. <i>Staphylococcus epidermidis</i>
<input type="radio"/>	C. <i>Escherichia coli</i>
<input type="radio"/>	D. <i>Neisseria gonorrhoeae</i>
<input type="radio"/>	E. <i>Streptococcus pneumoniae</i>

Next question

Septic arthritis - most common organism: *Staphylococcus aureus*

## Septic arthritis

### Overview

- most common organism overall is *Staphylococcus aureus*
- in young adults who are sexually active *Neisseria gonorrhoeae* should also be considered

### Management

- synovial fluid should be obtained before starting treatment
- intravenous antibiotics which cover Gram-positive cocci are indicated. The BNF currently recommends flucloxacillin or clindamycin if penicillin allergic
- antibiotic treatment is normally be given for several weeks (BNF states 6-12 weeks)
- needle aspiration should be used to decompress the joint
- surgical drainage may be needed if frequent needle aspiration is required

**Question 4 of 118**

Next

Low levels of which one of the following types of complement are associated with the development of systemic lupus erythematosus?

<input type="radio"/>	A. C4
<input type="radio"/>	B. C5
<input type="radio"/>	C. C6
<input type="radio"/>	D. C7
<input type="radio"/>	E. C8

Next question

SLE: C3 & C4 low

Low levels of C4a and C4b have been shown to be associated with an increased risk of developing systemic lupus erythematosus

**SLE: investigations**

## Immunology

- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)

## Monitoring

- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

Which one of the following is not a risk factor for developing osteoporosis?

<input type="radio"/>	A. Smoking
<input type="radio"/>	B. Obesity
<input type="radio"/>	C. Sedentary lifestyle
<input type="radio"/>	D. Premature menopause
<input type="radio"/>	E. Female sex

Next question

Low body mass, rather than obesity is associated with an increased risk of developing osteoporosis

### Osteoporosis: causes

#### Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

#### Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy\*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

\*research is ongoing as to whether warfarin is a risk factor

**Question 6 of 118**[Next](#)

A health trust in the United Kingdom which serves a population of 100,000 is planning services for patients with rheumatoid arthritis. How many of the population would be expected to have the disease?

<input type="radio"/>	A. 100
<input type="radio"/>	B. 300
<input type="radio"/>	C. 1,000
<input type="radio"/>	D. 2,000
<input type="radio"/>	E. 10,000

[Next question](#)

The prevalence of rheumatoid arthritis in the UK population is approximately 1%

**Rheumatoid arthritis: epidemiology****Epidemiology**

- peak onset = 30-50 years, although occurs in all age groups
- F:M ratio = 3:1
- prevalence = 1%
- some ethnic differences e.g. high in Native Americans
- associated with HLA-DR4 (especially Felty's syndrome)

**Question 7 of 118**

Next

A 31-year-old female intolerant of methotrexate is started on azathioprine for rheumatoid arthritis. Routine blood monitoring shows:

Hb	7.9 g/dl
Plt	$97 \times 10^9/l$
WBC	$2.7 \times 10^9/l$

Which of the following factors will predispose her to azathioprine toxicity?

- ☐ A. Cimetidine
- ☐ B. Rifampicin
- ☐ C. Fast acetylator status
- ☐ D. Thiopurine methyltransferase deficiency
- ☐ E. Alcohol excess

Next question

Azathioprine - check thiopurine methyltransferase deficiency (TPMT) before treatment

Thiopurine methyltransferase (TPMT) deficiency is present in about 1 in 200 people and predisposes to azathioprine related pancytopenia

**Azathioprine**

Azathioprine is metabolised to the active compound mercaptopurine, a purine analogue that inhibits purine synthesis. A thiopurine methyltransferase (TPMT) test may be needed to look for individuals prone to azathioprine toxicity.

Adverse effects include

- bone marrow depression
- nausea/vomiting
- pancreatitis

A significant interaction may occur with allopurinol and hence lower doses of azathioprine should be used.

**Question 8 of 118**

Next

Which of the following features are not typically seen in a patient with adult onset Still's disease?

<input type="radio"/>	A. Maculopapular rash
<input type="radio"/>	B. Rheumatoid factor
<input type="radio"/>	C. Pyrexia
<input type="radio"/>	D. High ferritin level
<input type="radio"/>	E. Lymphadenopathy

Next question

Adult onset Still's disease is typically rheumatoid factor negative

**Still's disease in adults**

Adult Still's disease

- typically affects 16-35 year olds

Features

- arthralgia
- elevated serum ferritin
- rash: salmon-pink, maculopapular
- pyrexia
- lymphadenopathy
- rheumatoid factor (RF) and anti-nuclear antibody (ANA) negative

### Question 9 of 118

Next

A 34-year-old woman with a history of antiphospholipid syndrome presents with a swollen and painful leg. Doppler ultrasound confirms a deep vein thrombosis (DVT). She had a previous DVT 4 months ago and was taking warfarin (with a target INR of 2-3) when the DVT occurred. How should her anticoagulation be managed?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Life-long warfarin, increase target INR to 3 - 4 |
| <input type="radio"/> | B. Add in life-long low-dose aspirin                |
| <input type="radio"/> | C. A further 6 months warfarin, target INR 2 - 3    |
| <input type="radio"/> | D. A further 6 months warfarin, target INR 3 - 4    |
| <input type="radio"/> | E. Life-long warfarin, target INR 2 - 3             |

Next question

The evidence base is scanty here but most clinicians would increase the target INR to 3-4 if a patient has had a further thrombosis with an INR of 2-3. Please see the BCSH guidelines

### Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

#### Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

#### Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3



**Question 10 of 118**

Next

A 41-year-old man with a past history of asthma presents with pain and weakness in his left hand. Examination findings are consistent with a left ulnar nerve palsy. Blood tests reveal an eosinophilia. Which one of the following antibodies is most likely to be present?

<input type="radio"/>	A. ANA
<input type="radio"/>	B. Anti-Scl70
<input type="radio"/>	C. pANCA
<input type="radio"/>	D. Antiphospholipid antibodies
<input type="radio"/>	E. cANCA

Next question

This patient has Churg-Strauss syndrome as evidenced by the asthma, mononeuritis and eosinophilia

**Churg-Strauss syndrome**

Churg-Strauss syndrome is an ANCA associated small-medium vessel vasculitis

**Features**

- asthma
- blood eosinophilia (e.g. > 10%)
- paranasal sinusitis
- mononeuritis multiplex
- pANCA positive in 60%

Leukotriene receptor antagonists may precipitate the disease

**Question 11 of 118**

Next

A 34-year-old intravenous drug user is admitted with a purpuric rash affecting her legs. Blood tests reveal the following:

Hb	11.4g/dl
Platelets	$489 \times 10^9/l$
WCC	$12.3 \times 10^9/l$
HCV PCR	positive
HBsAg	negative
Rheumatoid factor	positive
C3/C4	reduced

What is the most likely diagnosis?

<input type="radio"/>	A. Polyarteritis nodosa
<input type="radio"/>	B. Henoch-Schonlein purpura
<input type="radio"/>	C. Wegener's granulomatosis
<input checked="" type="radio"/>	D. Cryoglobulinaemia
<input type="radio"/>	E. Systemic lupus erythematosus

Next question

Hepatitis C infection is associated with type II (mixed) cryoglobulinaemia, suggested by the purpuric rash, positive rheumatoid factor and reduced complement levels

**Cryoglobulinaemia**

Immunoglobulins which undergo reversible precipitation at 4 deg C, dissolve when warmed to 37 deg C. One third of cases are idiopathic

Three types

- type I (25%): monoclonal
- type II (25%): mixed monoclonal and polyclonal: usually with RF
- type III (50%): polyclonal: usually with RF

Type I

- monoclonal - IgG or IgM

- associations: multiple myeloma, Waldenström macroglobulinaemia

## Type II

- mixed monoclonal and polyclonal: usually with RF
- associations: hepatitis C, RA, Sjogren's, lymphoma

## Type III

- polyclonal: usually with RF
- associations: RA, Sjogren's

## Symptoms (if present in high concentrations)

- Raynaud's only seen in type I
- cutaneous: vascular purpura, distal ulceration, ulceration
- arthralgia
- renal involvement (diffuse glomerulonephritis)

## Tests

- low complement (esp. C4)
- high ESR

## Treatment

- immunosuppression
- plasmapheresis

A 59-year-old man with a history of gout presents with a swollen and painful first metatarsophalangeal joint. He currently takes allopurinol 400mg od as gout prophylaxis. What should happen to his allopurinol therapy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Stop and recommence 4 weeks after acute inflammation has settled |
| <input type="radio"/> | B. Reduce allopurinol to 100mg od until acute attack has settled    |
| <input type="radio"/> | C. Stop and switch to colchicine prophylaxis                        |
| <input type="radio"/> | D. Stop and recommence 2 weeks after acute inflammation has settled |
| <input type="radio"/> | E. Continue allopurinol in current dose                             |

[Next question](#)

### Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450  $\mu\text{mol/l}$ )

#### Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

#### Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300  $\mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

#### Indications for allopurinol\*

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

## Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

\*patients with Lesch-Nyhan syndrome often take allopurinol for life

**Question 13 of 118**

Next

A 34-year-old is diagnosed with chronic fatigue syndrome. Which one of the following interventions is most useful?

<input type="radio"/>	A. Graded exercise therapy
<input type="radio"/>	B. Psychodynamic psychotherapy
<input type="radio"/>	C. Graded physiotherapy
<input type="radio"/>	D. Advice to avoid alcohol and caffeine
<input type="radio"/>	E. Low-dose fluoxetine

Next question

**Chronic fatigue syndrome**

Diagnosed after at least 4 months of disabling fatigue affecting mental and physical function more than 50% of the time in the absence of other disease which may explain symptoms

**Epidemiology**

- more common in females
- past psychiatric history has not been shown to be a risk factor

Fatigue is the central feature, other recognised features include

- sleep problems, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep-wake cycle
- muscle and/or joint pains
- headaches
- painful lymph nodes without enlargement
- sore throat
- cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding
- physical or mental exertion makes symptoms worse
- general malaise or 'flu-like' symptoms
- dizziness
- nausea
- palpitations

**Investigation**

- NICE guidelines suggest carrying out a large number of screening blood tests to exclude other pathology e.g. FBC, U&E, LFT, glucose, TFT, ESR, CRP, calcium, CK, ferritin\*, coeliac screening and also urinalysis

## Management

- cognitive behaviour therapy - very effective, number needed to treat = 2
- graded exercise therapy - a formal supervised program, not advice to go to the gym
- 'pacing' - organising activities to avoid tiring
- low-dose amitriptyline may be useful for poor sleep
- referral to a pain management clinic if pain is a predominant feature

Better prognosis in children

\*children and young people only

### Question 14 of 118

Next

A 68-year-old female presents with a two week history of intermittent headaches and lethargy. Blood tests reveal the following:

ESR	67 mm/hr
-----	----------

What is the most likely diagnosis?

<input type="radio"/>	A. Polymyalgia rheumatica
<input type="radio"/>	B. Cluster headaches
<input type="radio"/>	C. Polyarteritis nodosa
<input type="radio"/>	D. Migraine
<input type="radio"/>	E. Temporal arteritis

Next question

This is a classic history of temporal arteritis. Treatment should be started immediately with high dose steroids (e.g. prednisolone 1mg/kg/day) to reduce the chance of visual loss

### Temporal arteritis

Temporal arteritis is large vessel vasculitis which overlaps with polymyalgia rheumatica (PMR). Histology shows changes which characteristically 'skips' certain sections of affected artery whilst damaging others.

#### Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- headache (found in 85%)
- jaw claudication (65%)
- visual disturbances secondary to anterior ischemic optic neuropathy
- tender, palpable temporal artery
- features of PMR: aching, morning stiffness in proximal limb muscles (not weakness)
- also lethargy, depression, low-grade fever, anorexia, night sweats

#### Investigations

- raised inflammatory markers: ESR > 50 mm/hr (note ESR < 30 in 10% of patients). CRP may also be elevated
- temporal artery biopsy: skip lesions may be present
- note creatine kinase and EMG normal

#### Treatment



- high-dose prednisolone - there should be a dramatic response, if not the diagnosis should be reconsidered
- urgent ophthalmology review. Patients with visual symptoms should be seen the same-day by an ophthalmologist. Visual damage is often irreversible

Which one of the following cytokines is the most important in the pathophysiology of rheumatoid arthritis?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. IFN-beta               |
| <input type="radio"/> | B. IFN-alpha              |
| <input type="radio"/> | C. IL-4                   |
| <input type="radio"/> | D. Tumour necrosis factor |
| <input type="radio"/> | E. IL-2                   |

Next question

Rheumatoid arthritis - TNF is key in pathophysiology

### Tumour necrosis factor

Tumour necrosis factor (TNF) is a pro-inflammatory cytokine with multiple roles in the immune system

TNF is secreted mainly by macrophages and has a number of effects on the immune system, acting mainly in a paracrine fashion:

- activates macrophages and neutrophils
- acts as costimulator for T cell activation
- key mediator of body's response to Gram negative septicaemia
- similar properties to IL-1
- anti-tumour effect (e.g. phospholipase activation)

TNF-alpha binds to both the p55 and p75 receptor. These receptors can induce apoptosis. It also cause activation of NFkB

Endothelial effects include increase expression of selectins and increased production of platelet activating factor, IL-1 and prostaglandins

TNF promotes the proliferation of fibroblasts and their production of protease and collagenase. It is thought fragments of receptors act as binding points in serum

Systemic effects include pyrexia, increased acute phase proteins and disordered metabolism leading to cachexia

TNF is important in the pathogenesis of rheumatoid arthritis - TNF blockers (e.g. infliximab, etanercept) are now licensed for treatment of severe rheumatoid

## TNF blockers

- infliximab: monoclonal antibody, IV administration
- etanercept: fusion protein that mimics the inhibitory effects of naturally occurring soluble TNF receptors, subcutaneous administration
- adalimumab: monoclonal antibody, subcutaneous administration
- adverse effects of TNF blockers include reactivation of latent tuberculosis and demyelination

Infliximab is also used in active Crohn's disease unresponsive to steroids

**Question 16 of 118**

Next

A 54-year-old female is reviewed in the rheumatology clinic due to dry eyes and arthralgia. A diagnosis of primary Sjogren's syndrome is suspected. Which one of the following features is least associated with this condition?

<input type="radio"/>	A. Renal tubular acidosis
<input type="radio"/>	B. Xerostomia
<input type="radio"/>	C. Sensory polyneuropathy
<input type="radio"/>	D. Dilated cardiomyopathy
<input type="radio"/>	E. Raynaud's phenomenon

Next question

**Sjogren's syndrome**

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

**Features**

- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

**Investigation**

- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

**Management**

- artificial saliva and tears
- pilocarpine may stimulate saliva production

Which one of the following statements regarding systemic lupus erythematosus is true?

<input type="radio"/>	A. It is linked with HLA A5
<input type="radio"/>	B. Onset is typically between 20-40 years old
<input type="radio"/>	C. It is more common in Caucasians
<input type="radio"/>	D. The female:male ratio is 3:1
<input type="radio"/>	E. The incidence has decreased in the past 30 years

Next question

## Systemic lupus erythematosus

### Epidemiology

- much more common in females (F:M = 9:1)
- more common in Afro-Caribbeans\* and Asian communities
- onset is usually 20-40 years
- incidence has risen substantially during the past 50 years (3 fold using American College of Rheumatology criteria)

### Pathophysiology

- autoimmune disease
- associated with HLA B8, DR2, DR3
- thought to be caused by immune system dysregulation leading to immune complex formation
- immune complex deposition can affect any organ including the skin, joints, kidneys and brain

\*It is said that the incidence in black Africans is much lower than in black Americans - the reasons for this are unclear

**Question 18 of 118**

Next

A 45-year-old female with a history of rheumatoid arthritis presents to the Emergency Department with a two day history of a hot, painful, swollen right elbow joint. What is the most appropriate management?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Joint aspiration             |
| <input type="radio"/> | B. Start infliximab             |
| <input type="radio"/> | C. Oral high-dose prednisolone  |
| <input type="radio"/> | D. Short course of methotrexate |
| <input type="radio"/> | E. Depomedrone injection        |

Next question

Joint aspiration is mandatory in all patients with a hot, swollen joint to rule out septic arthritis. If this was excluded in the above patient then intra-articular or system steroid therapy may be considered.

**Septic arthritis**

## Overview

- most common organism overall is *Staphylococcus aureus*
- in young adults who are sexually active *Neisseria gonorrhoeae* should also be considered

## Management

- synovial fluid should be obtained before starting treatment
- intravenous antibiotics which cover Gram-positive cocci are indicated. The BNF currently recommends flucloxacillin or clindamycin if penicillin allergic
- antibiotic treatment is normally be given for several weeks (BNF states 6-12 weeks)
- needle aspiration should be used to decompress the joint
- surgical drainage may be needed if frequent needle aspiration is required

A 45-year-old man presents with a painful swelling on the posterior aspect of his elbow. There is no history of trauma. On examination an erythematous tender swelling is noted. What is the most likely diagnosis?

- ☐ A. Synovial cyst
- ☐ B. Haemarthrosis
- ☐ C. Septic arthritis
- ☐ D. Gout
- ☐ E. Olecranon bursitis

[Next question](#)

## Elbow pain

The table below details some of the characteristic features of conditions causing elbow pain:

<b>Lateral epicondylitis (tennis elbow)</b>	<p>Features</p> <ul style="list-style-type: none"> <li>• pain and tenderness localised to the lateral epicondyle</li> <li>• pain worse on resisted wrist extension with the elbow extended or supination of the forearm with the elbow extended</li> <li>• episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks</li> </ul>
<b>Medial epicondylitis (golfer's elbow)</b>	<p>Features</p> <ul style="list-style-type: none"> <li>• pain and tenderness localised to the medial epicondyle</li> <li>• pain is aggravated by wrist flexion and pronation</li> <li>• symptoms may be accompanied by numbness / tingling in the 4th and 5th finger due to ulnar nerve involvement</li> </ul>
<b>Radial tunnel syndrome</b>	<p>Most commonly due to compression of the posterior interosseous branch of the radial nerve. It is thought to be a result of overuse.</p> <p>Features</p> <ul style="list-style-type: none"> <li>• symptoms are similar to lateral epicondylitis making it difficult to diagnose</li> <li>• however, the pain tends to be around 4-5 cm distal to the lateral epicondyle</li> <li>• symptoms may be worsened by extending the elbow and pronating the forearm</li> </ul>
<b>Cubital tunnel syndrome</b>	<p>Due to the compression of the ulnar nerve.</p> <p>Features</p> <ul style="list-style-type: none"> <li>• initially intermittent tingling in the 4th and 5th finger</li> <li>• may be worse when the elbow is resting on a firm surface or flexed for extended periods</li> <li>• later numbness in the 4th and 5th finger with associated weakness</li> </ul>
<b>Olecranon bursitis</b>	<p>Swelling over the posterior aspect of the elbow. There may be associated pain, warmth and erythema. It typically affects middle-aged male patients.</p>

Which one of the following features is least commonly seen in drug-induced lupus?

<input type="radio"/>	A. Glomerulonephritis
<input type="radio"/>	B. Arthralgia
<input type="radio"/>	C. Myalgia
<input type="radio"/>	D. Malar rash
<input type="radio"/>	E. Pleurisy

Next question

Glomerulonephritis is unusual in drug-induced lupus

### Drug-induced lupus

In drug-induced lupus not all the typical features of systemic lupus erythematosus are seen, with renal and nervous system involvement being unusual. It usually resolves on stopping the drug

#### Features

- arthralgia
- myalgia
- skin (e.g. malar rash) and pulmonary involvement (e.g. pleurisy) are common
- ANA positive in 100%, dsDNA negative
- anti-histone antibodies are found in 80-90%
- anti-Ro, anti-Smith positive in around 5%

#### Causes

- procainamide
- isoniazid
- minocycline
- hydralazine
- chlorpromazine
- anti-epileptics: phenytoin



Which of the following is associated with a good prognosis in rheumatoid arthritis?

<input type="radio"/>	A. Rheumatoid factor negative
<input type="radio"/>	B. HLA DR4
<input type="radio"/>	C. Anti-CCP antibodies
<input type="radio"/>	D. Rheumatoid nodules
<input type="radio"/>	E. Insidious onset

Next question

### Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.

**Question 22 of 118**

Next

A 64-year-old man with chronic kidney disease stage 3 secondary to type 2 diabetes mellitus presents with pain and swelling at the right first metatarsophalangeal joint. On examination the joint is hot, erythematous and tender to touch, although he can still flex the big toe. What is the most appropriate initial management?

<input type="radio"/>	A. Colchicine
<input type="radio"/>	B. Prednisolone
<input type="radio"/>	C. Co-codamol 30/500
<input type="radio"/>	D. Allopurinol
<input type="radio"/>	E. Indomethacin

Next question

Colchicine is useful in patients with renal impairment who develop gout as NSAIDs are relatively contraindicated. The BNF advises to reduce the dose by up to 50% if creatinine clearance is less than 50 ml/min and to avoid if creatinine clearance is less than 10 ml/min.

Co-codamol 30/500 may be used as an adjunct but would not provide relief as monotherapy.

Prednisolone is an option but would adversely affect his diabetic control.

**Gout: management**

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450  $\mu\text{mol/l}$ )

**Acute management**

- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

**Allopurinol prophylaxis - see indications below**

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300  $\mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol\*

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

#### Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

\*patients with Lesch-Nyhan syndrome often take allopurinol for life

A 25-year-old woman presents with a three day history of dysuria and a painful left knee. During the review of symptoms she mentions a bout of diarrhoea and crampy abdominal pain three weeks ago. She is normally fit and well and takes no regular medication. Her father died of colorectal cancer in his sixth decade. On examination the left knee is red, swollen and hot to touch. What is the most likely diagnosis?

- ☐ A. Reactive arthritis secondary to *Salmonella* spp.
- ☐ B. Reactive arthritis secondary to *Chlamydia trachomatis*
- ☐ C. Rheumatoid arthritis
- ☐ D. Ulcerative colitis
- ☐ E. Gonococcal arthritis

[Next question](#)

Urethritis + arthritis + conjunctivitis = reactive arthritis

Two of the classic three features of reactive arthritis (urethritis, arthritis and conjunctivitis) are present in this patient. The family history of colorectal cancer is of no particular significance. Symptoms of reactive arthritis typically appear 1-4 weeks following the initial infection, in this case a diarrhoeal illness.

### Reactive arthritis

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA).

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint.

#### Epidemiology

- post-STI form much more common in men (e.g. 10:1)
- post-dysenteric form equal sex incidence

The table below shows the organisms that are most commonly associated with reactive arthritis:

Post-dysenteric form	Post-STI form
<i>Shigella flexneri</i> <i>Salmonella typhimurium</i> <i>Salmonella enteritidis</i> <i>Yersinia enterocolitica</i>	<i>Chlamydia trachomatis</i>

## Management

- symptomatic: analgesia, NSAIDS, intra-articular steroids
- sulfasalazine and methotrexate are sometimes used for persistent disease
- symptoms rarely last more than 12 months

**Question 24 of 118**

Next

An autoantibody screen reveals that a patient is positive for anti-Jo 1 antibodies. What is the most likely underlying diagnosis?

<input type="radio"/>	A. Limited cutaneous systemic sclerosis
<input type="radio"/>	B. Mixed connective tissue disease
<input type="radio"/>	C. Dermatomyositis
<input type="radio"/>	D. Polymyositis
<input type="radio"/>	E. Diffuse cutaneous systemic sclerosis

Next question

Anti-Jo 1 antibodies are more commonly seen in polymyositis than dermatomyositis

**Extractable nuclear antigens**

## Overview

- specific nuclear antigens
- usually associated with being ANA positive

## Examples

- anti-Ro: Sjogren's syndrome, SLE, congenital heart block
- anti-La: Sjogren's syndrome
- anti-Jo 1: polymyositis
- anti-scl-70: diffuse cutaneous systemic sclerosis
- anti-centromere: limited cutaneous systemic sclerosis

Which one of the following is least recognised as a risk factor for developing osteoporosis?

<input type="radio"/>	A. Cushing's syndrome
<input type="radio"/>	B. Turner's syndrome
<input type="radio"/>	C. Hyperparathyroidism
<input type="radio"/>	D. Hypothyroidism
<input type="radio"/>	E. Diabetes mellitus

Next question

Hyperthyroidism is associated with an increased risk of osteoporosis. Patients with hypothyroidism who take excessive amounts of levothyroxine may also be at risk of osteoporosis

### Osteoporosis: causes

#### Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

#### Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy\*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

\*research is ongoing as to whether warfarin is a risk factor

A 43-year-old woman presents with right-sided elbow pain. This has been present for the past month and she reports no obvious trigger. On examination she reports pain when the wrist is extended whilst the elbow is extended. What is the most likely diagnosis?

<input type="radio"/>	A. Cubital tunnel syndrome
<input type="radio"/>	B. Lateral epicondylitis
<input type="radio"/>	C. Carpal tunnel syndrome
<input type="radio"/>	D. Medial epicondylitis
<input type="radio"/>	E. Pronator syndrome

[Next question](#)

### Lateral epicondylitis

Lateral epicondylitis typically follows unaccustomed activity such as house painting or playing tennis ('tennis elbow'). It is most common in people aged 45-55 years and typically affects the dominant arm.

#### Features

- pain and tenderness localised to the lateral epicondyle
- pain worse on wrist extension against resistance with the elbow extended or supination of the forearm with the elbow extended
- episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks

#### Management options

- advice on avoiding muscle overload
- simple analgesia
- steroid injection
- physiotherapy



A 57-year-old man presents with pain in his right knee. An x-ray shows osteoarthritis. He has no past medical history of note. What is the most suitable treatment option for the management of his pain?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Oral diclofenac with omeprazole |
| <input type="radio"/> | B. Oral glucosamine                |
| <input type="radio"/> | C. Oral diclofenac                 |
| <input type="radio"/> | D. Oral ibuprofen                  |
| <input type="radio"/> | E. Oral paracetamol                |

[Next question](#)

Osteoarthritis - paracetamol + topical NSAIDs (if knee/hand) first-line

Oral NSAIDs should be used second line in osteoarthritis due to their adverse effect profile

### Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with NSAIDs and COX-2 inhibitors. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

A 31-year-old woman presents as her fingers intermittently turn white and become painful. She describes the fingers first turning white, then blue and finally red. This is generally worse in the winter months but it is present all year round. Wearing gloves does not help. Clinical examination of her hands, other joints and skin is unremarkable. Which one of the following treatments may be beneficial?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Amitriptyline |
| <input type="radio"/> | B. Aspirin       |
| <input type="radio"/> | C. Pregabalin    |
| <input type="radio"/> | D. Propranolol   |
| <input type="radio"/> | E. Nifedipine    |

[Next question](#)

This lady has Raynaud's disease.

### Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

**Question 29 of 118**

Next

A 79-year-old man presents with a history of lower back pain and right hip pain. Blood tests reveal the following:

Calcium	2.20 mmol/l
Phosphate	0.8 mmol/l
ALP	890 u/L

What is the most likely diagnosis?

- ☐ A. Primary hyperparathyroidism
- ☐ B. Chronic kidney disease
- ☐ C. Osteomalacia
- ☐ D. Osteoporosis
- ☐ E. Paget's disease

Next question

Paget's disease - old man, bone pain, raised ALP

The normal calcium and phosphate combined with a raised alkaline phosphate points to a diagnosis of Paget's

**Paget's disease of the bone**

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors

- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic

- bone pain (e.g. pelvis, lumbar spine, femur)
- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium\* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity, fracture, periarticular Paget's

- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

#### Complications

- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure

\*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

A 25-year-old man presents with back pain. Which one of the following may suggest a diagnosis of ankylosing spondylitis?

<input type="radio"/>	A. Rapid onset
<input type="radio"/>	B. Gets worse following exercise
<input type="radio"/>	C. Bone tenderness
<input type="radio"/>	D. Pain at night
<input type="radio"/>	E. Improves with rest

[Next question](#)

### Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

#### Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

#### Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

#### Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

Perinuclear antineutrophil cytoplasmic antibodies (pANCA) are most strongly associated with which condition?

<input type="radio"/>	A. Goodpasture's syndrome
<input type="radio"/>	B. Churg-Strauss syndrome
<input type="radio"/>	C. Polyarteritis nodosa
<input type="radio"/>	D. Wegener's granulomatosis
<input type="radio"/>	E. Autoimmune hepatitis

Next question

cANCA = Wegener's; pANCA = Churg-Strauss + others

## ANCA

There are two main types of anti-neutrophil cytoplasmic antibodies (ANCA) - cytoplasmic (cANCA) and perinuclear (pANCA)

For the exam, remember:

- cANCA - Wegener's granulomatosis
- pANCA - Churg-Strauss syndrome + others (see below)

### cANCA

- most common target serine proteinase 3 (PR3)
- some correlation between cANCA levels and disease activity
- Wegener's granulomatosis, positive in > 90%
- microscopic polyangiitis, positive in 40%

### pANCA

- most common target is myeloperoxidase (MPO)
- cannot use level of pANCA to monitor disease activity
- associated with immune crescentic glomerulonephritis (positive in c. 80% of patients)
- microscopic polyangiitis, positive in 50-75%
- Churg-Strauss syndrome, positive in 60%
- primary sclerosing cholangitis, positive in 60-80%
- Wegener's granulomatosis, positive in 25%

Other causes of positive ANCA (usually pANCA)

- inflammatory bowel disease (UC > Crohn's)
- connective tissue disorders: RA, SLE, Sjogren's
- autoimmune hepatitis

The presence of anti-cyclic citrullinated peptide antibody is suggestive of which one of the following conditions?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Systemic lupus erythematosus |
| <input type="radio"/> | B. Rheumatoid arthritis         |
| <input type="radio"/> | C. Type 1 diabetes mellitus     |
| <input type="radio"/> | D. Addison's disease            |
| <input type="radio"/> | E. Dermatomyositis              |

Next question

Anti-cyclic citrullinated peptide antibodies are associated with rheumatoid arthritis

Anti-cyclic citrullinated peptide antibody may be detectable up to 10 years before the development of rheumatoid arthritis. It may therefore play a key role in the future of rheumatoid arthritis, allowing early detection of patients suitable for aggressive anti-TNF therapy. It has a sensitivity similar to rheumatoid factor (70-80%, see below) with a much higher specificity of 90-95%.

### Rheumatoid factor

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG

RF can be detected by either

- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:

- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy



A 27-year-old woman presents with painful genital ulceration. She has had recurrent attacks for the past four years. Oral aciclovir has had little effect on the duration of her symptoms. She has also noticed for the past year almost weekly attacks of mouth ulcers which again are slow to heal. Her only past medical history of note is being treated for thrombophlebitis two years ago. What is the most likely diagnosis?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Behcet's syndrome            |
| <input type="radio"/> | B. Polyarteritis nodosa         |
| <input type="radio"/> | C. Systemic lupus erythematosus |
| <input type="radio"/> | D. Sarcoidosis                  |
| <input type="radio"/> | E. Herpes simplex virus type 2  |

[Next question](#)

### Behcet's syndrome

Behcet's syndrome is a complex multisystem disorder associated with presumed autoimmune mediated inflammation of the arteries and veins. The precise aetiology has yet to be elucidated however. The classic triad of symptoms are oral ulcers, genital ulcers and anterior uveitis

#### Epidemiology

- more common in the eastern Mediterranean (e.g. Turkey)
- more common in men (complicated gender distribution which varies according to country. Overall, Behcet's is considered to be more common and more severe in men)
- tends to affect young adults (e.g. 20 - 40 years old)
- associated with HLA B5\* and MICA6 allele
- c. 30% of patients have a positive family history

#### Features

- classically: 1) oral ulcers 2) genital ulcers 3) anterior uveitis
- thrombophlebitis
- arthritis
- neurological involvement (e.g. aseptic meningitis)
- GI: abdo pain, diarrhoea, colitis
- erythema nodosum, DVT

#### Diagnosis

- no definitive test
- diagnosis based on clinical findings
- positive pathergy test is suggestive (puncture site following needle prick becomes inflamed with small pustule forming)

\*more specifically HLA B51, a split antigen of HLA B5

Which one of the following statements regarding the 2010 American College of Rheumatology / European League Against Rheumatism classification criteria for rheumatoid arthritis is correct?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | <b>A.</b> A score of 7 out of 10 is sufficient to diagnose definite rheumatoid arthritis                                  |
| <input type="radio"/> | <b>B.</b> Inflammatory markers such as CRP and ESR are not part of the diagnostic criteria                                |
| <input type="radio"/> | <b>C.</b> Patients must have either a positive rheumatoid factor or a positive anti-cyclic citrullinated peptide antibody |
| <input type="radio"/> | <b>D.</b> Large joint arthritis is more relevant than small joint arthritis   |
| <input type="radio"/> | <b>E.</b> Gender is part of the scoring system  |

[Next question](#)

### Rheumatoid arthritis: diagnosis

NICE have stated that clinical diagnosis is more important than criteria such as those defined by the American College of Rheumatology.

#### 2010 American College of Rheumatology criteria

Target population. Patients who

- 1) have at least 1 joint with definite clinical synovitis
- 2) with the synovitis not better explained by another disease

Classification criteria for rheumatoid arthritis (add score of categories A-D; a score of 6/10 is needed definite rheumatoid arthritis)

Key

- RF = rheumatoid factor
- ACPA = anti-cyclic citrullinated peptide antibody

A. Joint involvement		
	1 large joint	0
	2 - 10 large joints	1
	1 - 3 small joints (with or without involvement of large joints)	2
	4 - 10 small joints (with or without involvement of large joints)	3
	10 joints (at least 1 small joint)	5

<b>B. Serology (at least 1 test result is needed for classification)</b>	
	Negative RF and negative ACPA 0
	Low-positive RF or low-positive ACPA 2
	High-positive RF or high-positive ACPA 3
<b>C. Acute-phase reactants (at least 1 test result is needed for classification)</b>	
	Normal CRP and normal ESR 0
	Abnormal CRP or abnormal ESR 1
<b>D. Duration of symptoms</b>	
	< 6 weeks 0
	> 6 weeks 1

A 56-year-old lady is referred to rheumatology clinic due to severe Raynaud's phenomenon associated with arthralgia of the fingers. On examination you note shiny and tight skin of the fingers with a number of telangiectasia on the upper torso and face. She is also currently awaiting a gastroscopy to investigate heartburn. Which one of the following antibodies is most specific for the underlying condition?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Anti-Jo 1 antibodies       |
| <input type="radio"/> | B. Rheumatoid factor          |
| <input type="radio"/> | C. Anti-Scl-70 antibodies     |
| <input type="radio"/> | D. Anti-centromere antibodies |
| <input type="radio"/> | E. Anti-nuclear factor        |

[Next question](#)

Limited (**central**) systemic sclerosis = anti-**centromere** antibodies

This lady has some features of CREST syndrome. Although ANA is positive in 90% of patients with systemic sclerosis, anti-centromere antibodies are the most specific test for limited cutaneous systemic sclerosis

### Systemic sclerosis

Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

Limited cutaneous systemic sclerosis

- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasia

Diffuse cutaneous systemic sclerosis

- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

## Scleroderma (without internal organ involvement)

- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear

## Antibodies

- ANA positive in 90%
- RF positive in 30%
- anti-scl-70 antibodies associated with diffuse cutaneous systemic sclerosis
- anti-centromere antibodies associated with limited cutaneous systemic sclerosis

Which one of the following is true regarding the investigation of a patient with dermatomyositis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Creatine kinase is characteristically normal |
| <input type="radio"/> | B. Muscle biopsy is contraindicated             |
| <input type="radio"/> | C. Anti-Jo-1 antibodies are usually negative    |
| <input type="radio"/> | D. Antinuclear antibodies are always negative   |
| <input type="radio"/> | E. EMG is normal                                |

Next question

Anti-Jo-1 antibodies are more common in polymyositis than dermatomyositis

### Dermatomyositis: investigations and management

#### Investigations

- elevated creatine kinase
- EMG
- muscle biopsy
- ANA positive in 60%
- anti-Jo-1 antibodies are not commonly seen in dermatomyositis - they are more common in polymyositis where they are seen in a pattern of disease associated with lung involvement, Raynaud's and fever
- anti-Mi-2 antibodies are highly specific for dermatomyositis, but are only seen in around 25% of patients

#### Management

- prednisolone

Which one of the following statements concerning discoid lupus is correct?

<input type="radio"/>	A. Commonly progresses to SLE
<input type="radio"/>	B. Causes non-scarring alopecia
<input type="radio"/>	C. Characterised by follicular keratin plugs
<input type="radio"/>	D. Is rarely photosensitive
<input type="radio"/>	E. Typically presents in older males

Next question

Discoid lupus erythematosus is characterised by follicular keratin plugs

### Discoid lupus erythematosus

Discoid lupus erythematosus is a benign disorder generally seen in younger females. It very rarely progresses to systemic lupus erythematosus (in less than 5% of cases). Discoid lupus erythematosus is characterised by follicular keratin plugs and is thought to be autoimmune in aetiology

#### Features

- erythematous, raised rash, sometimes scaly
- may be photosensitive
- more common on face, neck, ears and scalp
- lesions heal with atrophy, scarring (may cause scarring alopecia), and pigmentation

#### Management

- topical steroid cream
- oral antimalarials may be used second-line e.g. hydroxychloroquine
- avoid sun exposure

**Question 38 of 118**

Next

A 31-year-old female with a history of SLE gives birth following a 39 week pregnancy. The newborn is noted to be bradycardic. Which one of the following autoantibodies are associated with congenital heart block?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Anti-Ro    |
| <input type="radio"/> | B. Anti-Sm    |
| <input type="radio"/> | C. Anti-RNP   |
| <input type="radio"/> | D. Anti-dsDNA |
| <input type="radio"/> | E. Anti-Jo 1  |

Next question

SLE - antibodies associated with congenital heart block = anti-Ro

**SLE: pregnancy**

## Overview

- risk of maternal autoantibodies crossing placenta
- leads to condition termed neonatal lupus erythematosus
- neonatal complications include congenital heart block
- strongly associated with anti-Ro (SSA) antibodies



**Question 39 of 118**

Next

A 45-year-old woman with a history of primary Sjogren's syndrome is reviewed in clinic. Her main problem is a dry mouth, which unfortunately has not responded to artificial saliva. Which one of the following medications is most likely to be beneficial?

<input type="radio"/>	A. Rivastigmine
<input type="radio"/>	B. Neostigmine
<input type="radio"/>	C. Clonidine
<input type="radio"/>	D. Atropine
<input type="radio"/>	E. Pilocarpine

Next question

**Sjogren's syndrome**

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

**Features**

- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

**Investigation**

- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

**Management**

- artificial saliva and tears
- pilocarpine may stimulate saliva production

**Question 40 of 118**

Next

A 45-year-old woman is referred to rheumatology outpatients with a 4 month history of joint pains, myalgia and generalised lethargy. An autoantibody screen reveals she is ANA positive and anti-ribonucleoprotein positive. The creatine kinase is elevated at 525. What is the most likely diagnosis?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Systemic lupus erythematosus    |
| <input type="radio"/> | B. Mixed connective tissue disease |
| <input type="radio"/> | C. Polymyositis                    |
| <input type="radio"/> | D. Dermatomyositis                 |
| <input type="radio"/> | E. CREST syndrome                  |

Next question

Anti-ribonuclear protein (anti-RNP) = mixed connective tissue disease

**Mixed connective tissue disease**

Features of SLE, systemic sclerosis and polymyositis

Anti-RNP positive

**Question 41 of 118**

Next

A 57-year-old man with a history of ischaemic heart disease presents with a hot, erythematous and painful left 1st metatarsophalangeal joint. The attack settles following a course of non-steroidal anti-inflammatories. He currently takes aspirin 75 mg od for secondary prevention of ischaemic heart disease. What should happen regarding his medication?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Switch aspirin to clopidogrel     |
| <input type="radio"/> | B. Continue aspirin at current dose  |
| <input type="radio"/> | C. Increase aspirin dose to 300mg od |
| <input type="radio"/> | D. Switch aspirin to dipyridamole    |
| <input type="radio"/> | E. Stop aspirin                      |

Next question

Aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - please see the British Society for Rheumatology guidelines for more details.

**Gout: drug causes**

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

**Drug causes**

- thiazides, furosemide
- alcohol
- cytotoxic agents
- pyrazinamide

Osteopetrosis is due to a defect in:

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Osteoclast function                   |
| <input type="radio"/> | B. PTH receptors                         |
| <input type="radio"/> | C. Osteoblast function                   |
| <input type="radio"/> | D. Calcium resorption in proximal tubule |
| <input type="radio"/> | E. Calcium absorption                    |

Next question

## Osteopetrosis

### Overview

- aka marble bone disease
- rare disorder of defective osteoclast function resulting in failure of normal bone resorption
- stem cell transplant and interferon-gamma have been used for treatment

Each one of the following is seen in reactive arthritis, except:

<input type="radio"/>	A. Urethritis
<input type="radio"/>	B. Keratoderma blenorrhagica
<input type="radio"/>	C. Conjunctivitis
<input type="radio"/>	D. Aseptic meningoencephalitis
<input type="radio"/>	E. Circinate balanitis

Next question

### Reactive arthritis: features

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA).

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint.

#### Features

- typically develops within 4 weeks of initial infection - symptoms generally last around 4-6 months
- arthritis is typically an asymmetrical oligoarthritis of lower limbs
- dactylitis
- symptoms of urethritis
- eye: conjunctivitis (seen in 50%), anterior uveitis
- skin: circinate balanitis (painless vesicles on the coronal margin of the prepuce), keratoderma blenorrhagica (waxy yellow/brown papules on palms and soles)

Around 25% of patients have recurrent episodes whilst 10% of patients develop chronic disease

Which of the following is not a recognised cause of Raynaud's phenomenon?

<input type="radio"/>	A. Oral contraceptive pill
<input type="radio"/>	B. Cervical rib
<input type="radio"/>	C. Type I cryoglobulinaemia
<input type="radio"/>	D. Pizotifen
<input type="radio"/>	E. Scleroderma

Next question

Ergotamine rather than pizotifen is associated with Raynaud's phenomenon

### Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

A 54-year-old man with a history of type 2 diabetes mellitus presents with a history of right shoulder pain. On examination there is limited movement of the right shoulder in all directions. What is the most likely diagnosis?

<input type="radio"/>	A. Adhesive capsulitis
<input type="radio"/>	B. Dermatomyositis
<input type="radio"/>	C. Avascular necrosis
<input type="radio"/>	D. Lhermitte's syndrome
<input type="radio"/>	E. Diabetic amyotrophy

[Next question](#)

Diabetic amyotrophy affects the lower limbs

### Adhesive capsulitis

Adhesive capsulitis (frozen shoulder) is a common cause of shoulder pain. It is most common in middle-aged patients. The aetiology of frozen shoulder is not fully understood.

#### Associations

- diabetes mellitus: up to 20% of diabetics may have an episode of frozen shoulder

#### Features

- external rotation is affected more than internal rotation or abduction
- both active and passive movement are affected
- patients typically have a painful freezing phase, an adhesive phase and a recovery phase
- bilateral in up to 20% of patients
- the episode typically lasts between 6 months and 2 years

#### Management

- no single intervention has been shown to improve outcome in the long-term
- treatment options include NSAIDs, physiotherapy, oral corticosteroids and intra-articular corticosteroids

**Question 46 of 118**

Next

A 54-year-old woman who has had two Colle's fractures in the past three years has a DEXA scan:

	<b>T-score</b>
<b>L2-4</b>	-1.4
<b>Femoral neck</b>	-2.7

What does the scan show?

- ☐ A. Osteoporosis in both the vertebrae and femoral neck
- ☐ B. Osteoporosis in vertebrae, osteopaenia in femoral neck
- ☐ C. Osteopaenia in both the vertebrae and femoral neck
- ☐ D. Osteopaenia in vertebrae, osteoporosis in femoral neck
- ☐ E. Normal bone density in vertebrae, osteoporosis in femoral neck

Next question

**Osteoporosis: DEXA scan****Basics**

- T score: based on bone mass of young reference population
- T score of -1.0 means bone mass of one standard deviation below that of young reference population
- Z score is adjusted for age, gender and ethnic factors

**T score**

- $> -1.0$  = normal
- $-1.0$  to  $-2.5$  = osteopaenia
- $< -2.5$  = osteoporosis



A 28-year-old man is investigated for recurrent lower back pain. A diagnosis of ankylosing spondylitis is suspected. Which one of the following investigations is most useful?

<input type="radio"/>	A. ESR
<input type="radio"/>	B. X-ray of the sacro-iliac joints
<input type="radio"/>	C. HLA-B27 testing
<input type="radio"/>	D. X-ray of the thoracic spine
<input type="radio"/>	E. CT of the lumbar spine

[Next question](#)

X-ray of the sacro-iliac joints is the most useful investigation for diagnosis and monitoring, but changes may not be seen for many years after the onset of symptoms

### Ankylosing spondylitis: investigation and management

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

#### Investigation

Inflammatory markers (ESR, CRP) are typically raised although normal levels do not exclude ankylosing spondylitis.

HLA-B27 is of little use in making the diagnosis as it is positive in:

- 90% of patients with ankylosing spondylitis
- 10% of normal patients

Plain x-ray of the sacroiliac joints is the most useful investigation in establishing the diagnosis. Radiographs may be normal early in disease, later changes include:

- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)
- chest x-ray: apical fibrosis

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints.

#### Management

Early diagnosis is now more important following the advent of anti-TNF therapy

- encourage regular exercise such as swimming
- NSAIDs
- physiotherapy
- the disease-modifying drugs which are used to treat rheumatoid arthritis (such as sulphasalazine) are only really useful if there is peripheral joint involvement
- TNF-alpha blockers such as etanercept and adalimumab are increasingly used. This approach for severe ankylosing spondylitis was supported by NICE in 2008

Which one of the following conditions is least associated with HLA-B27?

<input type="radio"/>	A. Reiter's syndrome
<input type="radio"/>	B. Psoriatic arthritis
<input type="radio"/>	C. Ankylosing spondylitis
<input type="radio"/>	D. Crohn's disease
<input type="radio"/>	E. Sacroiliitis

Next question

There is an indirect association between HLA-B27 and Crohn's as some patients may develop enteropathic arthritis, but this is the least common association of the above

### Seronegative spondyloarthropathies

Common features

- associated with HLA-B27
- rheumatoid factor negative - hence 'seronegative'
- peripheral arthritis, usually asymmetrical
- sacroiliitis
- enthesopathy: e.g. Achilles tendonitis, plantar fasciitis
- extra-articular manifestations: uveitis, pulmonary fibrosis (upper zone), amyloidosis, aortic regurgitation

Spondyloarthropathies

- ankylosing spondylitis
- psoriatic arthritis
- Reiter's syndrome (including reactive arthritis)
- enteropathic arthritis (associated with IBD)

**Question 49 of 118**

Next

You are doing the annual review of a 50-year-old woman who has rheumatoid arthritis. Which one of the following complications is most likely to occur as a result of her disease?

<input type="radio"/>	A. Chronic lymphocytic leukaemia
<input type="radio"/>	B. Hypertension
<input type="radio"/>	C. Colorectal cancer
<input type="radio"/>	D. Type 2 diabetes mellitus
<input type="radio"/>	E. Ischaemic heart disease

Next question

Rheumatoid arthritis: patients have an increased risk of IHD

**Rheumatoid arthritis: complications**

A wide variety of extra-articular complications occur in patients with rheumatoid arthritis (RA):

- respiratory: pulmonary fibrosis, pleural effusion, pulmonary nodules, bronchiolitis obliterans, methotrexate pneumonitis, pleurisy
- ocular: keratoconjunctivitis sicca (most common), episcleritis, scleritis, corneal ulceration, keratitis, steroid-induced cataracts, chloroquine retinopathy
- osteoporosis
- ischaemic heart disease: RA carries a similar risk to type 2 diabetes mellitus
- increased risk of infections
- depression

Less common

- Felty's syndrome (RA + splenomegaly + low white cell count)
- amyloidosis

A 54-year-old male presents with weakness of his upper arms. On examination he is found to have a macular rash over his back and the extensor aspects of his upper arms. He is a heavy smoker and his sodium is 121 mmol/l. What is the most likely underlying diagnosis?

<input type="radio"/>	A. Addison's disease
<input type="radio"/>	B. Polymyositis
<input type="radio"/>	C. Overlap syndrome
<input checked="" type="radio"/>	D. Dermatomyositis
<input type="radio"/>	E. Hypothyroidism

[Next question](#)

This man may have an underlying small cell lung cancer causing Syndrome of Inappropriate Antidiuretic Hormone Secretion.

## Dermatomyositis

### Overview

- inflammatory disorder causing symmetrical, proximal muscle weakness and characteristic skin lesions
- may be idiopathic or associated with connective tissue disorders or underlying malignancy (typically lung cancer, found in 20-25% - more if patient older)
- polymyositis is a variant of the disease where skin manifestations are not prominent

### Skin features

- photosensitive
- macular rash over back and shoulder
- heliotrope rash in the periorbital region
- Gottron's papules - roughened red papules over extensor surfaces of fingers
- nail fold capillary dilatation

### Other features

- proximal muscle weakness +/- tenderness
- Raynaud's
- respiratory muscle weakness
- interstitial lung disease: e.g. Fibrosing alveolitis or organising pneumonia
- dysphagia, dysphonia

Which of the following findings is not typical in a patient with antiphospholipid syndrome?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Prolonged APTT                |
| <input type="radio"/> | B. Thrombocytosis                |
| <input type="radio"/> | C. Recurrent venous thrombosis   |
| <input type="radio"/> | D. Recurrent arterial thrombosis |
| <input type="radio"/> | E. Livedo reticularis            |

Next question

Antiphospholipid syndrome: arterial/venous thrombosis, miscarriage, livedo reticularis

Thrombocytopenia is associated with antiphospholipid syndrome

### Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

#### Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

#### Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

Which one of the following is least recognised as a risk factor for developing osteoporosis?

<input type="radio"/>	A. Multiple myeloma
<input type="radio"/>	B. Rheumatoid arthritis
<input type="radio"/>	C. Long-term phenytoin therapy
<input type="radio"/>	D. Chronic renal failure
<input type="radio"/>	E. Diabetes mellitus

Next question

Long-term phenytoin therapy may cause enhanced vitamin D metabolism leading to osteomalacia, rather than osteoporosis

### Osteoporosis: causes

#### Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

#### Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy\*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

\*research is ongoing as to whether warfarin is a risk factor



Which one of the following is least recognised in polyarteritis nodosa?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Cytoplasmic-antineutrophil cytoplasmic antibodies |
| <input type="radio"/> | B. Hypertension                                      |
| <input type="radio"/> | C. Mononeuritis multiplex                            |
| <input type="radio"/> | D. Pyrexia   |
| <input type="radio"/> | E. Renal failure                                     |

Next question

Perinuclear-antineutrophil cytoplasmic antibodies are found in around 20% of patients

### Polyarteritis nodosa

Polyarteritis nodosa (PAN) is a vasculitis affecting medium-sized arteries with necrotizing inflammation leading to aneurysm formation. PAN is more common in middle-aged men and is associated with hepatitis B infection

#### Features

- fever, malaise, arthralgia
- hypertension
- mononeuritis multiplex, sensorimotor polyneuropathy
- haematuria, renal failure
- testicular pain
- abdominal pain (e.g. from mesenteric ischaemia)
- perinuclear-antineutrophil cytoplasmic antibodies (ANCA) are found in around 20% of patients with 'classic' PAN

A 51-year-old male presents with an acute onset of swelling and pain in his right knee. Aspiration shows negatively birefringent crystals with no organisms seen. His pain fails to settle with NSAIDs. What is the most appropriate next step in his management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Repeat joint aspiration and intra-articular depomedrol |
| <input type="radio"/> | B. Allopurinol  |
| <input type="radio"/> | C. IV flucloxacillin                                      |
| <input type="radio"/> | D. Diuretics  |
| <input type="radio"/> | E. Low dose methotrexate                                  |

[Next question](#)

### Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450  $\mu\text{mol/l}$ )

#### Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

#### Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300  $\mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

#### Indications for allopurinol\*

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

## Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

\*patients with Lesch-Nyhan syndrome often take allopurinol for life

Which of the following is least likely to be associated with ankylosing spondylitis?

<input type="radio"/>	A. Apical fibrosis
<input type="radio"/>	B. Achilles tendonitis
<input type="radio"/>	C. Amyloidosis
<input type="radio"/>	D. Achalasia
<input type="radio"/>	E. Heart block

Next question

Ankylosing spondylitis features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis

Achalasia is not a recognised association of ankylosing spondylitis

### Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

#### Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

#### Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

## Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

A 54-year-old man presents to the Emergency Department with a 2 day history of a swollen, painful left knee. Aspirated joint fluid shows calcium pyrophosphate crystals. Which of the following blood tests is most useful in revealing an underlying cause?

<input type="radio"/>	A. Transferrin saturation
<input type="radio"/>	B. ACTH
<input type="radio"/>	C. ANA
<input type="radio"/>	D. Serum ferritin
<input type="radio"/>	E. LDH

[Next question](#)

This is a typical presentation of pseudogout. An elevated transferrin saturation may indicate haemochromatosis, a recognised cause of pseudogout

A high ferritin level is also seen in haemochromatosis but can be raised in a variety of infective and inflammatory processes, including pseudogout, as part of an acute phase response

### Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

#### Risk factors

- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

#### Features

- knee, wrist and shoulders most commonly affected
- joint aspiration: weakly-positively birefringent rhomboid shaped crystals
- x-ray: chondrocalcinosis

#### Management

- aspiration of joint fluid, to exclude septic arthritis
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

A 41-year-old female presents with lethargy and pain all over her body. This has been present for the past six months and is often worse when she is stressed or cold. Clinical examination is unremarkable other than a large number of tender points throughout her body. A series of blood tests including an autoimmune screen, inflammatory markers and thyroid function are normal. Given the likely diagnosis, which one of the following is not helpful in management?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Amitriptyline                 |
| <input type="radio"/> | B. Trigger point injections      |
| <input type="radio"/> | C. Cognitive behavioural therapy |
| <input type="radio"/> | D. Exercise programme            |
| <input type="radio"/> | E. Paracetamol                   |

[Next question](#)

A recent JAMA paper supported the use of anti-depressants in fibromyalgia

Treatment of fibromyalgia syndrome with antidepressants: a meta-analysis; 2009 Jan 14;301(2):198-209

## Fibromyalgia

Fibromyalgia is a syndrome characterised by widespread pain throughout the body with tender points at specific anatomical sites. The cause of fibromyalgia is unknown.

### Epidemiology

- women are 10 times more likely to be affected
- typically presents between 30-50 years old

### Features

- pain: at multiple site, sometimes 'pain all over'
- lethargy
- sleep disturbance, headaches, dizziness are common

Diagnosis is clinical and sometimes refers to the American College of Rheumatology classification criteria which lists 9 pairs of tender points on the body. If a patient is tender in at least 11 of these 18 points it makes a diagnosis of fibromyalgia more likely

The management of fibromyalgia is often difficult and needs to be tailored to the individual patient. A psychosocial and multidisciplinary approach is helpful. Unfortunately there is currently a paucity of evidence and guidelines to guide practice. The following is partly based on consensus guidelines from the European League against Rheumatism (EULAR) published in 2007.

- explanation
- exercise programme
- cognitive behavioural therapy
- anti-depressants: amitriptyline



A 47-year-old female is referred to the rheumatology clinic due to cold fingers. Which connective tissue disease is most strongly associated with Raynaud's phenomenon?

<input type="radio"/>	A. Systemic lupus erythematosus
<input type="radio"/>	B. Rheumatoid arthritis
<input type="radio"/>	C. Systemic sclerosis
<input type="radio"/>	D. Sjogren's syndrome
<input type="radio"/>	E. Polyarteritis nodosa

Next question

Raynaud's phenomenon is associated with all the above conditions but is most strongly linked to systemic sclerosis. Around 2% of women and 6% of men with Raynaud's phenomenon develop systemic sclerosis

### Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

Which one of the following is the most common ocular manifestation of rheumatoid arthritis?

<input type="radio"/>	A. Scleritis
<input type="radio"/>	B. Episcleritis
<input type="radio"/>	C. Keratoconjunctivitis sicca
<input type="radio"/>	D. Corneal ulceration
<input type="radio"/>	E. Keratitis

Next question

Keratoconjunctivitis sicca is characterised by dry, burning and gritty eyes caused by decreased tear production

### Rheumatoid arthritis: ocular manifestations

Ocular manifestations of rheumatoid arthritis are common, with 25% of patients having eye problems

Ocular manifestations

- keratoconjunctivitis sicca (most common)
- episcleritis (erythema)
- scleritis (erythema and pain)
- corneal ulceration
- keratitis

Iatrogenic

- steroid-induced cataracts
- chloroquine retinopathy

Which one of the following drugs is least likely to cause gout?

<input type="radio"/>	A. Lithium
<input type="radio"/>	B. Bendrofluazide
<input type="radio"/>	C. Alcohol
<input type="radio"/>	D. Pyrazinamide
<input type="radio"/>	E. Furosemide

Next question

Lithium was actually used to treat gout in the 19th century

### Gout: drug causes

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Drug causes

- thiazides, furosemide
- alcohol
- cytotoxic agents
- pyrazinamide

**Question 61 of 118**

Next

A 39-year-old woman with a history of rheumatoid arthritis presents with a two day history of a red right eye. There is no itch or pain. Pupils are 3mm, equal and reactive to light. Visual acuity is 6/5 in both eyes. What is the most likely diagnosis?

<input type="radio"/>	A. Keratoconjunctivitis sicca
<input type="radio"/>	B. Scleritis
<input type="radio"/>	C. Glaucoma
<input type="radio"/>	D. Episcleritis
<input type="radio"/>	E. Anterior uveitis

Next question

Scleritis is painful, episcleritis is not painful

**Rheumatoid arthritis: ocular manifestations**

Ocular manifestations of rheumatoid arthritis are common, with 25% of patients having eye problems

**Ocular manifestations**

- keratoconjunctivitis sicca (most common)
- episcleritis (erythema)
- scleritis (erythema and pain)
- corneal ulceration
- keratitis

**Iatrogenic**

- steroid-induced cataracts
- chloroquine retinopathy

Which one of the following is most useful in the management of Familial Mediterranean Fever?

<input type="radio"/>	A. Prednisolone
<input type="radio"/>	B. Erythromycin
<input type="radio"/>	C. Cyclophosphamide
<input checked="" type="radio"/>	D. Colchicine
<input type="radio"/>	E. Benzylpenicillin

Next question

### Familial Mediterranean Fever

Familial Mediterranean Fever (FMF, also known as recurrent polyserositis) is an autosomal recessive disorder which typically presents by the second decade. It is more common in people of Turkish, Armenian and Arabic descent

Features - attacks typically last 1-3 days

- pyrexia
- abdominal pain (due to peritonitis)
- pleurisy
- pericarditis
- arthritis
- erysipeloid rash on lower limbs

Management

- colchicine may help

**Question 63 of 118**[Next](#)

A 64-year-old female is referred to rheumatology out-patients by her GP with a history of arthritis in both hands. Which one of the following x-ray findings would most favour a diagnosis of rheumatoid arthritis over other possible causes?

<input type="radio"/>	A. Loss of joint space
<input checked="" type="radio"/>	B. Periarticular osteopenia
<input type="radio"/>	C. Subchondral sclerosis
<input type="radio"/>	D. Osteophytes
<input type="radio"/>	E. Subchondral cysts

[Next question](#)

Periarticular osteopenia and osteoporosis would point towards a diagnosis of rheumatoid arthritis (RA). Loss of joint space is common in both RA and osteoarthritis

**Rheumatoid arthritis: x-ray changes****Early x-ray findings**

- loss of joint space
- juxta-articular osteoporosis
- soft-tissue swelling

**Late x-ray findings**

- periarticular erosions
- subluxation

**Question 64 of 118**

Next

A 33-year-old man who is suspected of having ankylosing spondylitis has a lumbar spine x-ray. Which one of the following features is most likely to be present?

<input type="radio"/>	A. Wedge shaped discs
<input type="radio"/>	B. Sclerosis
<input type="radio"/>	C. 'Rugger-Jersey' spine
<input type="radio"/>	D. Osteophytes
<input type="radio"/>	E. Subchondral cysts

Next question

Ankylosing spondylitis - x-ray findings: subchondral erosions, sclerosis and squaring of lumbar vertebrae

**Ankylosing spondylitis: features**

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

**Features**

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

**Clinical examination**

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

**Other features - the 'A's**

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation

- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)



A 40-year-old woman complains of a permanent 'funny-bone' sensation in her right elbow. This is accompanied by tingling in the little and ring finger. Her symptoms are worse when the elbow is bent for prolonged periods. What is the most likely diagnosis?

- ☐ A. Cubital tunnel syndrome
- ☐ B. Lateral epicondylitis
- ☐ C. Medial epicondylitis
- ☐ D. Median nerve entrapment syndrome
- ☐ E. Radial tunnel syndrome

[Next question](#)

### Elbow pain

The table below details some of the characteristic features of conditions causing elbow pain:

<b>Lateral epicondylitis (tennis elbow)</b>	<p>Features</p> <ul style="list-style-type: none"> <li>• pain and tenderness localised to the lateral epicondyle</li> <li>• pain worse on resisted wrist extension with the elbow extended or supination of the forearm with the elbow extended</li> <li>• episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks</li> </ul>
<b>Medial epicondylitis (golfer's elbow)</b>	<p>Features</p> <ul style="list-style-type: none"> <li>• pain and tenderness localised to the medial epicondyle</li> <li>• pain is aggravated by wrist flexion and pronation</li> <li>• symptoms may be accompanied by numbness / tingling in the 4th and 5th finger due to ulnar nerve involvement</li> </ul>
<b>Radial tunnel syndrome</b>	<p>Most commonly due to compression of the posterior interosseous branch of the radial nerve. It is thought to be a result of overuse.</p> <p>Features</p> <ul style="list-style-type: none"> <li>• symptoms are similar to lateral epicondylitis making it difficult to diagnose</li> <li>• however, the pain tends to be around 4-5 cm distal to the lateral epicondyle</li> <li>• symptoms may be worsened by extending the elbow and pronating the forearm</li> </ul>
<b>Cubital tunnel syndrome</b>	<p>Due to the compression of the ulnar nerve.</p> <p>Features</p> <ul style="list-style-type: none"> <li>• initially intermittent tingling in the 4th and 5th finger</li> <li>• may be worse when the elbow is resting on a firm surface or flexed for extended periods</li> <li>• later numbness in the 4th and 5th finger with associated weakness</li> </ul>
<b>Olecranon bursitis</b>	<p>Swelling over the posterior aspect of the elbow. There may be associated pain, warmth and erythema. It typically affects middle-aged male patients.</p>

**Question 66 of 118**[Next](#)

A 41-year-old man presents with persistent fatigue for the past 8 months. Which one of the following features is least consistent with a diagnosis of chronic fatigue syndrome?

<input type="radio"/>	A. Dizziness
<input type="radio"/>	B. Painful lymph nodes without enlargement
<input type="radio"/>	C. Having a busy day improves the symptoms
<input type="radio"/>	D. Palpitations
<input type="radio"/>	E. Headaches

[Next question](#)

Physical or mental exertion usually makes the symptoms worse

**Chronic fatigue syndrome**

Diagnosed after at least 4 months of disabling fatigue affecting mental and physical function more than 50% of the time in the absence of other disease which may explain symptoms

**Epidemiology**

- more common in females
- past psychiatric history has not been shown to be a risk factor

Fatigue is the central feature, other recognised features include

- sleep problems, such as insomnia, hypersomnia, unrefreshing sleep, a disturbed sleep-wake cycle
- muscle and/or joint pains
- headaches
- painful lymph nodes without enlargement
- sore throat
- cognitive dysfunction, such as difficulty thinking, inability to concentrate, impairment of short-term memory, and difficulties with word-finding
- physical or mental exertion makes symptoms worse
- general malaise or 'flu-like' symptoms
- dizziness
- nausea
- palpitations

**Investigation**

- NICE guidelines suggest carrying out a large number of screening blood tests to exclude other pathology e.g. FBC, U&E, LFT, glucose, TFT, ESR, CRP, calcium, CK, ferritin\*, coeliac screening and also urinalysis

## Management

- cognitive behaviour therapy - very effective, number needed to treat = 2
- graded exercise therapy - a formal supervised program, not advice to go to the gym
- 'pacing' - organising activities to avoid tiring
- low-dose amitriptyline may be useful for poor sleep
- referral to a pain management clinic if pain is a predominant feature

Better prognosis in children

\*children and young people only

Which one of the following is least associated with Behcet's syndrome?

<input type="radio"/>	A. Mouth ulcers
<input type="radio"/>	B. Genital ulcers
<input type="radio"/>	C. Conjunctivitis
<input type="radio"/>	D. Deep vein thrombosis
<input type="radio"/>	E. Aseptic meningitis

Next question

Oral ulcers + genital ulcers + anterior uveitis = Behcet's

Mouth ulcers, genital ulcers, deep vein thrombosis and aseptic meningitis are all recognised features of Behcet's syndrome

Ocular involvement is the most feared complication of Behcet's syndrome. Conjunctivitis is seen rarely and is much less common than anterior uveitis. Other ocular problems seen include retinal vasculitis, iridocyclitis and chorioretinitis

### Behcet's syndrome

Behcet's syndrome is a complex multisystem disorder associated with presumed autoimmune mediated inflammation of the arteries and veins. The precise aetiology has yet to be elucidated however. The classic triad of symptoms are oral ulcers, genital ulcers and anterior uveitis

#### Epidemiology

- more common in the eastern Mediterranean (e.g. Turkey)
- more common in men (complicated gender distribution which varies according to country. Overall, Behcet's is considered to be more common and more severe in men)
- tends to affect young adults (e.g. 20 - 40 years old)
- associated with HLA B5\* and MICA6 allele
- c. 30% of patients have a positive family history

#### Features

- classically: 1) oral ulcers 2) genital ulcers 3) anterior uveitis
- thrombophlebitis
- arthritis
- neurological involvement (e.g. aseptic meningitis)
- GI: abdo pain, diarrhoea, colitis

- erythema nodosum, DVT

## Diagnosis

- no definitive test
- diagnosis based on clinical findings
- positive pathergy test is suggestive (puncture site following needle prick becomes inflamed with small pustule forming)

\*more specifically HLA B51, a split antigen of HLA B5

A 31-year-old patient is diagnosed with rheumatoid arthritis. Which of the following is associated with a good prognosis?

<input type="radio"/>	A. Being a non-smoker
<input type="radio"/>	B. Erosions on x-ray first developing 18 months after diagnosis
<input type="radio"/>	C. Sudden onset
<input type="radio"/>	D. Being diagnosed aged 35 years
<input type="radio"/>	E. Anti-CCP antibodies

[Next question](#)

### Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.

A 44-year-old female with a history of Raynaud's phenomenon is reviewed in the rheumatology clinic. She is currently being investigated for dysphagia. On examination she is noted to have tight, shiny skin over her fingers. Which one of the following complications she most likely to develop?

<input type="radio"/>	A. Early onset dementia
<input type="radio"/>	B. Erythema nodosum
<input type="radio"/>	C. Malabsorption
<input type="radio"/>	D. Constrictive pericarditis
<input type="radio"/>	E. Erosive joint disease

[Next question](#)

This patient is likely to have CREST syndrome, a subtype of limited cutaneous systemic sclerosis. Malabsorption can develop in these patients secondary to bacterial overgrowth of the sclerosed small intestine

Whilst diffuse systemic sclerosis is associated with more severe and rapid internal organ involvement it is also seen in the limited form.

### Systemic sclerosis

Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

Limited cutaneous systemic sclerosis

- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia

Diffuse cutaneous systemic sclerosis

- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

Scleroderma (without internal organ involvement)

- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear

#### Antibodies

- ANA positive in 90%
- RF positive in 30%
- anti-scl-70 antibodies associated with diffuse cutaneous systemic sclerosis
- anti-centromere antibodies associated with limited cutaneous systemic sclerosis



Which one of the following features is least typical of polymyalgia rheumatica?

<input type="radio"/>	A. Elevated creatine kinase
<input type="radio"/>	B. Low-grade fever
<input type="radio"/>	C. Morning stiffness in proximal limb muscles
<input type="radio"/>	D. Polyarthralgia
<input type="radio"/>	E. Anorexia

Next question

## Polymyalgia rheumatica

### Pathophysiology

- overlaps with temporal arteritis
- histology shows vasculitis with giant cells, characteristically 'skips' certain sections of affected artery whilst damaging others
- muscle bed arteries affected most in polymyalgia rheumatica

### Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- aching, morning stiffness in proximal limb muscles (not weakness)
- also mild polyarthralgia, lethargy, depression, low-grade fever, anorexia, night sweats

### Investigations

- ESR > 40 mm/hr
- note CK and EMG normal
- reduced CD8+ T cells

### Treatment

- prednisolone e.g. 15mg/od - dramatic response

A 61-year-old man is noted to have thickened patches of skin over his knuckles and extensor surfaces consistent with Gottron's papules. His creatinine kinase levels are also elevated. A diagnosis of dermatomyositis is suspected. Which one of the following types of autoantibody is most specific for this condition?

<input type="radio"/>	A. Anti-scl-70 antibodies
<input type="radio"/>	B. Anti-Jo-1 antibodies
<input type="radio"/>	C. Anti-nuclear antibodies
<input type="radio"/>	D. Anti-Mi-2 antibodies
<input type="radio"/>	E. Anti-centromere bodies

[Next question](#)

Dermatomyositis antibodies: ANA most common, anti-Mi-2 most specific

## Dermatomyositis: investigations and management

### Investigations

- elevated creatine kinase
- EMG
- muscle biopsy
- ANA positive in 60%
- anti-Jo-1 antibodies are not commonly seen in dermatomyositis - they are more common in polymyositis where they are seen in a pattern of disease associated with lung involvement, Raynaud's and fever
- anti-Mi-2 antibodies are highly specific for dermatomyositis, but are only seen in around 25% of patients

### Management

- prednisolone

Which one of the following statements regarding ankylosing spondylitis is correct?

<input type="radio"/>	A. Schober's test assesses reduced chest expansion
<input type="radio"/>	B. HLA-B27 is positive in 50% of patients
<input type="radio"/>	C. Achilles tendonitis is a recognised association
<input type="radio"/>	D. It affects men twice as commonly as women
<input type="radio"/>	E. The typical age of presentation is between 40-50 years

Next question

HLA-B27 is positive in 90% of patients.

### Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

#### Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

#### Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

#### Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

A 54-year-old man is recovering following his first episode of gout. The pain and inflammation settled 4 days ago. He has no risk factors for the development of gout and there is no evidence of gouty tophi on examination. What is the most suitable point to start uric acid lowering therapy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Immediately  |
| <input type="radio"/> | B. If more than 6 episodes of gout in a 1 year period   |
| <input type="radio"/> | C. If one further attack of gout in the next 12 months  |
| <input type="radio"/> | D. 4 weeks after the initial attack of gout has settled |
| <input type="radio"/> | E. If more than 4 episodes of gout in a 1 year period   |

[Next question](#)

Gout: start allopurinol if  $\geq 2$  attacks in 12 month period

### Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid  $> 450 \mu\text{mol/l}$ )

#### Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

#### Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of  $< 300 \mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

#### Indications for allopurinol\*

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'

- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

#### Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

\*patients with Lesch-Nyhan syndrome often take allopurinol for life

Which one of the following conditions has polygenic inheritance?

<input type="radio"/>	A. Bartter's syndrome
<input type="radio"/>	B. Huntington disease
<input type="radio"/>	C. Ankylosing spondylitis
<input type="radio"/>	D. Fragile X syndrome
<input type="radio"/>	E. Von Willebrand's disease

Next question

### Ankylosing spondylitis: investigation and management

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

#### Investigation

Inflammatory markers (ESR, CRP) are typically raised although normal levels do not exclude ankylosing spondylitis.

HLA-B27 is of little use in making the diagnosis as it is positive in:

- 90% of patients with ankylosing spondylitis
- 10% of normal patients

Plain x-ray of the sacroiliac joints is the most useful investigation in establishing the diagnosis. Radiographs may be normal early in disease, later changes include:

- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)
- chest x-ray: apical fibrosis

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints.

#### Management

Early diagnosis is now more important following the advent of anti-TNF therapy

- encourage regular exercise such as swimming
- NSAIDs
- physiotherapy
- the disease-modifying drugs which are used to treat rheumatoid arthritis (such as sulphasalazine) are only really useful if there is peripheral joint involvement
- TNF-alpha blockers such as etanercept and adalimumab are increasingly used. This approach for severe ankylosing spondylitis was supported by NICE in 2008

**Question 75 of 118**

Next

A 47-year-old female presents with elbow pain. She has just spent the weekend painting the house. On examination there is localised pain around the lateral epicondyle and a diagnosis of lateral epicondylitis is suspected. Which one of the following movements would characteristically worsen the pain?

<input type="radio"/>	A. Resisted thumb flexion
<input type="radio"/>	B. Thumb extension
<input type="radio"/>	C. Flexion of the elbow
<input type="radio"/>	D. Pronation of the forearm with the elbow flexed
<input type="radio"/>	E. Resisted wrist extension with the elbow extended

Next question

Lateral epicondylitis: worse on resisted wrist extension/supination whilst elbow extended

**Lateral epicondylitis**

Lateral epicondylitis typically follows unaccustomed activity such as house painting or playing tennis ('tennis elbow'). It is most common in people aged 45-55 years and typically affects the dominant arm.

**Features**

- pain and tenderness localised to the lateral epicondyle
- pain worse on wrist extension against resistance with the elbow extended or supination of the forearm with the elbow extended
- episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks

**Management options**

- advice on avoiding muscle overload
- simple analgesia
- steroid injection
- physiotherapy



Approximately what percentage of patients with psoriasis develop an associated arthropathy?

<input type="radio"/>	A. 0.5%
<input type="radio"/>	B. 12-15%
<input type="radio"/>	C. 4-5%
<input type="radio"/>	D. 1%
<input type="radio"/>	E. 10%

Next question

### Psoriatic arthropathy

Psoriatic arthropathy correlates poorly with cutaneous psoriasis and often precedes the development of skin lesions. Around 10% of patients with skin lesions develop an arthropathy with males and females being equally affected

Types\*

- rheumatoid-like polyarthritis: (30-40%, most common type)
- asymmetrical oligoarthritis: typically affects hands and feet (20-30%)
- sacroilitis
- DIP joint disease (10%)
- arthritis mutilans (severe deformity fingers/hand, 'telescoping fingers')

Management

- treat as rheumatoid arthritis
- but better prognosis

\*Until recently it was thought asymmetrical oligoarthritis was the most common type, based on data from the original 1973 Moll and Wright paper. Please see the link for a comparison of more recent studies

You review a 48-year-old woman who is taking methotrexate for rheumatoid arthritis. Concurrent prescription of which other medication should be avoided?

<input type="radio"/>	A. Erythromycin
<input checked="" type="radio"/>	B. Trimethoprim
<input type="radio"/>	C. Sumatriptan
<input type="radio"/>	D. Lansoprazole
<input type="radio"/>	E. Sodium valproate

[Next question](#)

There is an increased risk of haematological toxicity when trimethoprim is prescribed alongside methotrexate.

### Methotrexate

Methotrexate is an antimetabolite which inhibits dihydrofolate reductase, an enzyme essential for the synthesis of purines and pyrimidines

#### Indications

- rheumatoid arthritis
- psoriasis
- acute lymphoblastic leukaemia

#### Adverse effects

- mucositis
- myelosuppression
- pneumonitis
- liver cirrhosis

#### Pregnancy

- women should avoid pregnancy for at least 3 months after treatment has stopped
- the BNF also advises that men using methotrexate need to use effective contraception for at least 3 months after treatment

#### Prescribing methotrexate

- methotrexate is a drug with a high potential for patient harm. It is therefore important that you are familiar with guidelines relating to its use

- methotrexate is taken weekly, rather than daily
- FBC, U&E and LFTs need to be regularly monitored. The Committee on Safety of Medicines recommend 'FBC and renal and LFTs before starting treatment and repeated weekly until therapy stabilised, thereafter patients should be monitored every 2-3 months'
- folic acid 5mg once weekly should be co-prescribed, taken more than 24 hours after methotrexate dose
- the starting dose of methotrexate is 7.5 mg weekly (source: BNF)
- only one strength of methotrexate tablet should be prescribed (usually 2.5 mg)
- avoid prescribing trimethoprim or cotrimoxazole concurrently - increases risk of marrow aplasia

**Question 78 of 118**

Next

A 68-year-old presents with a painful swollen left knee which has failed to settle after a weeks rest. There is no history of trauma. On examination he has a moderate sized effusion. A plain radiograph is reported as follows:

Some loss of joint space  
Linear calcification of the articular cartilage

What is the most likely diagnosis?

<input type="radio"/>	A. Pseudogout
<input type="radio"/>	B. Rheumatoid arthritis
<input type="radio"/>	C. Sarcoidosis
<input type="radio"/>	D. Gout
<input type="radio"/>	E. Osteoarthritis

Next question

This x-ray describes chondrocalcinosis. Non-specific changes such as loss of joint space are common in this age group and pseudogout itself may cause osteoarthritic-like changes.

**Pseudogout**

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

**Risk factors**

- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

**Features**

- knee, wrist and shoulders most commonly affected
- joint aspiration: weakly-positively birefringent rhomboid shaped crystals
- x-ray: chondrocalcinosis

**Management**

- aspiration of joint fluid, to exclude septic arthritis
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

A 69-year-old man presents with an acute episode of gout on his left first metatarsal-phalangeal joint. What is the most likely underlying mechanism?

- |                                  |   |
|----------------------------------|---|
| <input type="radio"/>            | A. Sedentary lifestyle                          |
| <input checked="" type="radio"/> | B. Decreased renal excretion of uric acid       |
| <input type="radio"/>            | C. Increased endogenous production of uric acid |
| <input type="radio"/>            | D. Starvation                                   |
| <input type="radio"/>            | E. Too much protein in diet                     |

[Next question](#)

The vast majority of gout is due to decreased renal excretion of uric acid

Decreased renal excretion of uric acid is thought to account for 90% of cases of primary gout. Secondary risk factors such as alcohol intake and medications should also be investigated

#### Gout: predisposing factors

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Decreased excretion of uric acid

- drugs\*: diuretics
- chronic kidney disease
- lead toxicity

Increased production of uric acid

- myeloproliferative/lymphoproliferative disorder
- cytotoxic drugs
- severe psoriasis

Lesch-Nyhan syndrome

- hypoxanthine-guanine phosphoribosyl transferase deficiency
- inheritance = x-linked recessive
- features: gout, renal failure, learning difficulties, head-banging

\*aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - the British Society for Rheumatology recommend it should be continued if required for cardiovascular prophylaxis

A 50-year-old man with no past medical history is investigated for ongoing back pain. He is found to have a vertebral collapse secondary to osteoporosis. What is the most appropriate test to determine the cause of his osteoporosis?

<input type="radio"/>	A. Thyroid function tests
<input type="radio"/>	B. Prostate specific antigen
<input type="radio"/>	C. Oestrogen level
<input type="radio"/>	D. Prolactin level
<input type="radio"/>	E. Testosterone level

[Next question](#)

Osteoporosis in a man - check testosterone

Whilst thyrotoxicosis is a known cause of osteoporosis, testosterone deficiency is much more likely in a middle-aged male

### Osteoporosis: causes

#### Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

#### Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy\*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

A 54-year-old farm worker presents for review. She has recently been diagnosed with osteoarthritis of the hand but has no other past medical history of note. Despite regular paracetamol she is still experiencing considerable pain, especially around the base of both thumbs. What is the most suitable next management step?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Add oral diclofenac + lansoprazole      |
| <input type="radio"/> | B. Switch paracetamol for co-codamol 8/500 |
| <input type="radio"/> | C. Add topical ibuprofen                   |
| <input type="radio"/> | D. Add oral ibuprofen                      |
| <input type="radio"/> | E. Add oral glucosamine                    |

Next question

Osteoarthritis - paracetamol + topical NSAIDs (if knee/hand) first-line

The 2008 NICE guidelines suggest the use of paracetamol and topical NSAIDs first-line

### Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with NSAIDs and COX-2 inhibitors. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended

- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness



A 24-year-old female is investigated for intermittent pain and swelling of the metacarpal phalangeal joints for the past 3 months. An x-ray shows loss of joint space and soft-tissue swelling. Rheumatoid factor is positive and a diagnosis of rheumatoid arthritis is made. What is the most appropriate management to slow disease progression?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Infliximab  |
| <input type="radio"/> | B. Rituximab   |
| <input type="radio"/> | C. Sulfasalazine   |
| <input type="radio"/> | D. Methotrexate + sulfasalazine + short-course of prednisolone |
| <input type="radio"/> | E. Diclofenac  |

[Next question](#)

The 2009 NICE guidelines recommend that patients with newly diagnosed active RA start a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids). Women of child-bearing age should be given effective contraception for the duration of treatment and for 3 months after methotrexate has been stopped.

### Rheumatoid arthritis: management

The management of rheumatoid arthritis (RA) has been revolutionised by the introduction of disease-modifying therapies in the past decade. NICE has issued a number of technology appraisals on the newer agents and released general guidelines in 2009.

Patients with evidence of joint inflammation should start a combination of disease-modifying drugs (DMARD) as soon as possible. Other important treatment options include analgesia, physiotherapy and surgery.

#### Initial therapy

- in the 2009 NICE guidelines it is recommend that patients with newly diagnosed active RA start a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids)

#### DMARDs

- methotrexate is the most widely used DMARD. Monitoring of FBC & LFTs is essential due to the risk of myelosuppression and liver cirrhosis. Other important side-effects include pneumonitis
- sulfasalazine
- leflunomide
- hydroxychloroquine

#### TNF-inhibitors

- the current indication for a TNF-inhibitor is an inadequate response to at least two DMARDs including methotrexate
- etanercept: recombinant human protein, acts as a decoy receptor for TNF- $\alpha$ , subcutaneous administration, can cause demyelination, risks include reactivation of tuberculosis
- infliximab: monoclonal antibody, binds to TNF- $\alpha$  and prevents it from binding with TNF receptors, intravenous administration, risks include reactivation of tuberculosis
- adalimumab: monoclonal antibody, subcutaneous administration

## Rituximab

- anti-CD20 monoclonal antibody, results in B-cell depletion
- two 1g intravenous infusions are given two weeks apart
- infusion reactions are common

## Abatacept

- fusion protein that modulates a key signal required for activation of T lymphocytes
- leads to decreased T-cell proliferation and cytokine production
- given as an infusion
- not currently recommended by NICE

A 40-year-old woman who is known to have systemic lupus erythematosus is reviewed with an exacerbation of wrist pain. Which one of the following is the most useful marker for monitoring disease activity?

<input type="radio"/>	A. C-reactive protein
<input type="radio"/>	B. C2 levels
<input type="radio"/>	C. Anti-nuclear antibody titres
<input type="radio"/>	D. Anti-dsDNA titres
<input type="radio"/>	E. Anti-Smith titres

[Next question](#)

## SLE: investigations

### Immunology

- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)

### Monitoring

- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

Which one of the following is not associated with carpal tunnel syndrome?

<input type="radio"/>	A. Tinel's sign
<input type="radio"/>	B. Compression of the median nerve
<input type="radio"/>	C. Wasting of the hypothenar eminence
<input type="radio"/>	D. Flexion of the wrist reproduces symptoms
<input type="radio"/>	E. Weakness of thumb abduction

Next question

### Carpal tunnel syndrome

Carpal tunnel syndrome is caused by compression of median nerve in the carpal tunnel.

#### History

- pain/pins and needles in thumb, index, middle finger
- unusually the symptoms may 'ascend' proximally
- patient shakes his hand to obtain relief, classically at night

#### Examination

- weakness of thumb abduction (abductor pollicis brevis)
- wasting of thenar eminence (NOT hypothenar)
- Tinel's sign: tapping causes paraesthesia
- Phalen's sign: flexion of wrist causes symptoms

#### Causes

- idiopathic
- pregnancy
- oedema e.g. heart failure
- lunate fracture
- rheumatoid arthritis

#### Electrophysiology

- motor + sensory: prolongation of the action potential

## Treatment

- corticosteroid injection
- wrist splints at night
- surgical decompression (flexor retinaculum division)

A 34-year-old kitchen worker presents with a two week history of pain in her right wrist. She has recently emigrated from Ghana and has no past medical history of note. On examination she is tender over the base of her right thumb and also over the radial styloid process. Ulnar deviation of the wrist recreates the pain. What is the most likely diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Rheumatoid arthritis                        |
| <input type="radio"/> | B. Osteoarthritis of the carpometacarpal joint |
| <input type="radio"/> | C. De Quervain's tenosynovitis                 |
| <input type="radio"/> | D. Carpal tunnel syndrome                      |
| <input type="radio"/> | E. Systemic lupus erythematosus                |

[Next question](#)

### De Quervain's tenosynovitis

De Quervain's tenosynovitis is a common condition in which the sheath containing the extensor pollicis brevis and abductor pollicis longus tendons is inflamed. It typically affects females aged 30 - 50 years old

#### Features

- pain on the radial side of the wrist
- tenderness over the radial styloid process
- abduction of the thumb against resistance is painful
- Finkelstein's test: with the thumb flexed across the palm of the hand, pain is reproduced by movement of the wrist into flexion and ulnar deviation

#### Management

- analgesia
- steroid injection
- immobilisation with a thumb splint (spica) may be effective
- surgical treatment is sometimes required

A 54-year-old man is diagnosed as having gout. You are discussing ways to help prevent future attacks. Which one of the following is most likely to precipitate an attack of gout?

<input type="radio"/>	A. Chocolate
<input type="radio"/>	B. Brazil nuts
<input type="radio"/>	C. Eggs
<input type="radio"/>	D. Sardines
<input type="radio"/>	E. Smoking

[Next question](#)

Foods to avoid include those high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

### Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450  $\mu\text{mol/l}$ )

#### Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

#### Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300  $\mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

#### Indications for allopurinol\*

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

## Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

\*patients with Lesch-Nyhan syndrome often take allopurinol for life



**Question 87 of 118**

Next

A 45-year-old man presents with a painful, swollen and red left middle toe. There is no history of trauma and his symptoms have been present for around a week. Which one of the following conditions is most associated with this presentation?

<input type="radio"/>	A. Diabetes mellitus
<input type="radio"/>	B. Systemic sclerosis
<input type="radio"/>	C. Rheumatoid arthritis
<input type="radio"/>	D. Bisphosphonate use
<input type="radio"/>	E. Psoriatic arthritis

Next question

**Dactylitis**

Dactylitis describes the inflammation of a digit (finger or toe).

Causes include:

- spondyloarthritis: e.g. Psoriatic and reactive arthritis
- sickle-cell disease
- other rare causes include tuberculosis, sarcoidosis and syphilis

A 27-year-old woman is referred to orthopaedics. Three years she had surgery and chemotherapy for thyroid cancer. Follow up scans to date have shown no evidence of any disease recurrence. For the past two months she has been experiencing gradually increasing pain in her right hip which is worse on exercising. On examination passive movement of the hip is painful in all directions, especially internal rotation. An x-ray ordered by her GP has been reported as normal. What is the most likely diagnosis?

<input type="radio"/>	A. Trochanteric bursitis
<input checked="" type="radio"/>	B. Avascular necrosis of the femoral head
<input type="radio"/>	C. Primary hyperparathyroidism
<input type="radio"/>	D. Metastatic deposits
<input type="radio"/>	E. Hypoparathyroidism

[Next question](#)

Initial x-rays are often normal in patients with avascular necrosis, but it would be unlikely that metastatic deposits significant enough to cause pain would not be shown.

### Avascular necrosis

Avascular necrosis (AVN) may be defined as death of bone tissue secondary to loss of the blood supply. This leads to bone destruction and loss of joint function. It most commonly affects the epiphysis of long bones such as the femur.

#### Causes

- long-term steroid use
- chemotherapy
- alcohol excess
- trauma

#### Features

- initially asymptomatic
- pain in the affected joint

#### Investigation

- plain x-ray findings may be normal initially
- MRI is the investigation of choice. It is more sensitive than radionuclide bone scanning

### Question 89 of 118

A 73-year-old man presents pain in his right thigh. This has been getting progressively worse for the past 9 months despite being otherwise well. An x-ray is reported as follows:

X-ray right femur	Radiolucency of subarticular region suggestive of osteolysis. Some areas of patchy sclerosis
-------------------	--

Bloods tests show:

Calcium	2.38 mmol/l
Phosphate	0.85 mmol/l
Alkaline phosphatase	544 u/L
Prostate specific antigen	4.4 ng/ml

What is the most appropriate action?

<input type="radio"/>	A. Vitamin D supplementation
<input type="radio"/>	B. Check serum testosterone
<input type="radio"/>	C. Referral to an orthopaedic surgeon
<input type="radio"/>	D. Referral to a urologist
<input type="radio"/>	E. IV bisphosphonates

[Next question](#)

This patient has Paget's disease as evidenced by an isolated rise in ALP and characteristic x-ray changes. As he has bone pain he should be treated with bisphosphonates. A PSA of 4.4 ng/ml is probably normal in a 73-year-old man and is certainly not consistent with metastatic prostate cancer

### Paget's disease of the bone

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors

- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic

- bone pain (e.g. pelvis, lumbar spine, femur)

- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium\* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity, fracture, periarticular Paget's

- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

### Complications

- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure

\*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

A 25-year-old man presents with a painful, swollen left knee. He returned 4 weeks ago from a holiday in Spain. There is no history of trauma and he has had no knee problems previously. On examination he has a swollen, warm left knee with a full range of movement. His ankle joints are also painful to move but there is no swelling. On the soles of both feet you notice a waxy yellow rash. What is the most likely diagnosis?

- |                       |                         |
|-----------------------|-------------------------|
| <input type="radio"/> | A. Rheumatoid arthritis |
| <input type="radio"/> | B. Psoriatic arthritis  |
| <input type="radio"/> | C. Gout                 |
| <input type="radio"/> | D. Reactive arthritis   |
| <input type="radio"/> | E. Gonococcal arthritis |

[Next question](#)

The rash on the soles is keratoderma blenorrhagica. His reactive arthritis may be secondary to either gastrointestinal infection or *Chlamydia*.

### Reactive arthritis: features

Reactive arthritis is one of the HLA-B27 associated seronegative spondyloarthropathies. It encompasses Reiter's syndrome, a term which described a classic triad of urethritis, conjunctivitis and arthritis following a dysenteric illness during the Second World War. Later studies identified patients who developed symptoms following a sexually transmitted infection (post-STI, now sometimes referred to as sexually acquired reactive arthritis, SARA).

Reactive arthritis is defined as an arthritis that develops following an infection where the organism cannot be recovered from the joint.

#### Features

- typically develops within 4 weeks of initial infection - symptoms generally last around 4-6 months
- arthritis is typically an asymmetrical oligoarthritis of lower limbs
- dactylitis
- symptoms of urethritis
- eye: conjunctivitis (seen in 50%), anterior uveitis
- skin: circinate balanitis (painless vesicles on the coronal margin of the prepuce), keratoderma blenorrhagica (waxy yellow/brown papules on palms and soles)

Around 25% of patients have recurrent episodes whilst 10% of patients develop chronic disease

A 24-year-old man is investigated for chronic back pain. Which one of the following would most suggest a diagnosis of ankylosing spondylitis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Reduced lateral flexion of the lumbar spine |
| <input type="radio"/> | B. Pain gets worse during the day              |
| <input type="radio"/> | C. Accentuated lumbar lordosis                 |
| <input type="radio"/> | D. Pain on straight leg raising                |
| <input type="radio"/> | E. Loss of thoracic kyphosis                   |

[Next question](#)

Reduced lateral flexion of the lumbar spine is one of the earliest signs of ankylosing spondylitis. There tends to be a loss of lumbar lordosis and an accentuated thoracic kyphosis in patients with ankylosing spondylitis

### Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

#### Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

#### Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

#### Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

**Question 92 of 118**

Next

A 45-year-old man who is known to have haemochromatosis presents with a swollen and painful right knee. An x-ray shows no fracture but extensive chondrocalcinosis. Given the likely diagnosis, which one of the following is most likely to present in the joint fluid?

<input type="radio"/>	A. Raised hyaluronic acid levels
<input type="radio"/>	B. Monosodium urate crystals
<input type="radio"/>	C. Bipyramidal oxalate crystals
<input type="radio"/>	D. Negatively birefringent calcium carbonate crystals
<input type="radio"/>	E. Positively birefringent rhomboid-shaped crystals

Next question

Pseudogout - positively birefringent rhomboid shaped crystals

**Pseudogout**

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

**Risk factors**

- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

**Features**

- knee, wrist and shoulders most commonly affected
- joint aspiration: weakly-positively birefringent rhomboid shaped crystals
- x-ray: chondrocalcinosis

**Management**

- aspiration of joint fluid, to exclude septic arthritis
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

Which of the following statements is true regarding psoriatic arthropathy?

<input type="radio"/>	A. Skin disease always precedes joint disease
<input type="radio"/>	B. Approximately one-third of patients with psoriasis eventually develop arthropathy
<input type="radio"/>	C. The mainstay of management is analgesia, physiotherapy and joint replacement
<input checked="" type="radio"/>	D. Males and females are equally affected
<input type="radio"/>	E. Arthritis mutilans is the most common subtype

Next question

Males and females are affected equally by psoriatic arthritis

### Psoriatic arthropathy

Psoriatic arthropathy correlates poorly with cutaneous psoriasis and often precedes the development of skin lesions. Around 10% of patients with skin lesions develop an arthropathy with males and females being equally affected

Types\*

- rheumatoid-like polyarthritis: (30-40%, most common type)
- asymmetrical oligoarthritis: typically affects hands and feet (20-30%)
- sacroilitis
- DIP joint disease (10%)
- arthritis mutilans (severe deformity fingers/hand, 'telescoping fingers')

Management

- treat as rheumatoid arthritis
- but better prognosis

\*Until recently it was thought asymmetrical oligoarthritis was the most common type, based on data from the original 1973 Moll and Wright paper. Please see the link for a comparison of more recent studies



Which one of the following is most recognised as a risk factor for developing osteoporosis?

<input type="radio"/>	A. Osteogenesis imperfecta
<input type="radio"/>	B. Marfan's syndrome
<input type="radio"/>	C. Myotonic dystrophy
<input type="radio"/>	D. Duchenne muscular dystrophy
<input type="radio"/>	E. Ehler-Danlos syndrome

Next question

### Osteoporosis: causes

#### Risk factors

- family history
- female sex
- increasing age
- deficient diet
- sedentary lifestyle
- smoking
- premature menopause
- low body weight
- Caucasians and Asians

#### Diseases which predispose

- endocrine: glucocorticoid excess (e.g. Cushing's, steroid therapy), hyperthyroidism, hypogonadism (e.g. Turner's, testosterone deficiency), growth hormone deficiency, hyperparathyroidism, diabetes mellitus
- multiple myeloma, lymphoma
- gastrointestinal problems: inflammatory bowel disease, malabsorption (e.g. Coeliacs), gastrectomy, liver disease
- rheumatoid arthritis
- long term heparin therapy\*
- chronic renal failure
- osteogenesis imperfecta, homocystinuria

\*research is ongoing as to whether warfarin is a risk factor

A 71-year-old man presents with an erythematous, swollen first metatarsophalangeal joint on the left foot. This is causing him considerable pain and he is having difficulty walking. He has never had any previous similar episodes. His past medical history includes atrial fibrillation and type 2 diabetes mellitus and his current medications are warfarin, metformin and simvastatin. What is the most appropriate treatment of this episode?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Intra-articular corticosteroid |
| <input type="radio"/> | B. Colchicine                     |
| <input type="radio"/> | C. Ibuprofen                      |
| <input type="radio"/> | D. Diclofenac                     |
| <input type="radio"/> | E. Prednisolone                   |

[Next question](#)

NSAIDs should be avoided in elderly patients taking warfarin due to the risk of a life-threatening gastrointestinal haemorrhage. Oral steroids are an option but would upset his diabetic control.

Whilst anticoagulation is not a contraindication to joint injection it would make this option less attractive

### Gout: management

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 450  $\mu\text{mol/l}$ )

#### Acute management

- NSAIDs
- intra-articular steroid injection
- colchicine has a slower onset of action. The main side-effect is diarrhoea
- if the patient is already taking allopurinol it should be continued

#### Allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled as it may precipitate a further attack if started too early
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300  $\mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

#### Indications for allopurinol\*

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'

- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

#### Lifestyle modifications

- reduce alcohol intake and avoid during an acute attack
- lose weight if obese
- avoid food high in purines e.g. Liver, kidneys, seafood, oily fish (mackerel, sardines) and yeast products

\*patients with Lesch-Nyhan syndrome often take allopurinol for life

**Question 96 of 118**[Next](#)

A 33-year-old female presents 6 weeks after the birth of her first child with a two-week history of polyarthralgia, fever and a skin rash. First-line investigations show:

ESR	45 mm/hour
-----	------------

What is the most likely diagnosis?

<input type="radio"/>	A. Polymorphic eruption of pregnancy
<input type="radio"/>	B. Systemic lupus erythematosus
<input type="radio"/>	C. Rheumatoid arthritis
<input type="radio"/>	D. Reactive arthritis
<input type="radio"/>	E. Pseudogout

[Next question](#)

Unlike many autoimmune diseases systemic lupus erythematosus (SLE) often becomes worse during pregnancy and the puerperium

**SLE: pregnancy****Overview**

- risk of maternal autoantibodies crossing placenta
- leads to condition termed neonatal lupus erythematosus
- neonatal complications include congenital heart block
- strongly associated with anti-Ro (SSA) antibodies

**Question 97 of 118**

Next

A 57-year-old woman with a history of polymyalgia rheumatica has been taking prednisolone 10 mg for the past 5 months. A DEXA scan is reported as follows:

L2 T-score	-1.6 SD
Femoral neck T-score	-1.7 SD

What is the most suitable management?

- ☐ A. No treatment
- ☐ B. Vitamin D + calcium supplementation + repeat DEXA scan in 6 months
- ☐ C. Vitamin D + calcium supplementation
- ☐ D. Vitamin D + calcium supplementation + hormone replacement therapy
- ☐ E. Vitamin D + calcium supplementation + oral bisphosphonate

Next question

This patient has been taking 10mg of prednisolone for the past 5 months and hence should be assessed for bone protection. The T score of less than -1.5 SD is an indication for a bisphosphonate. This should be co-prescribed with calcium + vitamin D.

**Osteoporosis: glucocorticoid-induced**

Patients who take the equivalent of prednisolone 7.5 mg or more each day for 3 months or longer should be assessed and where necessary given prophylactic treatment

Assessment for treatment - patients taking the equivalent of prednisolone 7.5 mg or more each day for 3 months, and one of the following

- are over the age of 65 years
- have a history of a fragility fracture
- have a T-score less than - 1.5 SD

Treatment

- first-line: oral bisphosphonate
- second-line: alfacalcidol or calcitriol

Which one of the following would not suggest an underlying connective tissue disorder in a patient with Raynaud's?

<input type="radio"/>	A. Unilateral symptoms
<input type="radio"/>	B. Digital ulcers
<input type="radio"/>	C. Presence of autoantibodies
<input type="radio"/>	D. Onset at 25 years old
<input type="radio"/>	E. Calcinosis

[Next question](#)

Raynaud's disease (i.e. primary) presents in young women with bilateral symptoms

## Raynaud's

Raynaud's phenomena may be primary (Raynaud's disease) or secondary (Raynaud's phenomenon)

Raynaud's disease typically presents in young women (e.g. 30 years old) with symmetrical attacks

Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

## Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

A 66-year-old female presents with pain at the base of her left thumb. She has no past medical history of note. On examination there is diffuse tenderness and swelling of her left first carpometacarpal joint. What is the most likely diagnosis?

<input type="radio"/>	A. Osteoarthritis
<input type="radio"/>	B. De Quervain's tenosynovitis
<input type="radio"/>	C. Gout
<input type="radio"/>	D. Rheumatoid arthritis
<input type="radio"/>	E. Primary hyperparathyroidism

[Next question](#)

The trapeziometacarpal joint (base of thumb) is the most common site of hand osteoarthritis.

### Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with NSAIDs and COX-2 inhibitors. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended
- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness



A 66-year-old female is on long-term prednisolone therapy for polymyalgia rheumatica. What is the most appropriate protection against osteoporosis?

<input type="radio"/>	A. Hormone replacement therapy
<input type="radio"/>	B. Calcitonin
<input type="radio"/>	C. Oral bisphosphonate
<input type="radio"/>	D. Calcium and vitamin D
<input type="radio"/>	E. Hip-protectors

[Next question](#)

Oral bisphosphonate therapy is recommended for patients older than 65 years who have taken, or who are likely to remain on oral corticosteroids for more than 3 months

### Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

#### Clinical uses

- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metastases

#### Adverse effects

- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw
- increased risk of atypical stress fractures of the proximal femoral shaft in patients taking alendronate

The BNF suggests the following counselling for patients taking oral bisphosphonates

- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

A 54-year-old woman is reviewed. She was discharged from the psychiatric ward around 5 weeks ago following an admission for an acute psychotic episode. Her psychotic symptoms have settled on risperidone but unfortunately she has now developed a dry mouth and arthralgia in both hands. A number of blood tests are requested:

Rheumatoid factor	Positive
Anti-Ro	Positive
Anti-Smith	Negative
ANA	Positive
C4	Low

What is the most likely diagnosis?

- ☐ A. Systemic lupus erythematosus
- ☐ B. Sarcoidosis
- ☐ C. Drug-induced lupus erythematosus
- ☐ D. Rheumatoid arthritis
- ☐ E. Sjogren's syndrome

Next question

Risperidone (unlike chlorpromazine) is not a common trigger of lupus. Anti-Ro is positive in around 70% of patients with Sjogren's syndrome compared to around 10% of patients with rheumatoid arthritis

### Sjogren's syndrome

Sjogren's syndrome is an autoimmune disorder affecting exocrine glands resulting in dry mucosal surfaces. It may be primary (PSS) or secondary to rheumatoid arthritis or other connective tissue disorders, where it usually develops around 10 years after the initial onset. Sjogren's syndrome is much more common in females (ratio 9:1). There is a marked increased risk of lymphoid malignancy (40-60 fold)

#### Features

- dry eyes: keratoconjunctivitis sicca
- dry mouth
- vaginal dryness
- arthralgia
- Raynaud's, myalgia
- sensory polyneuropathy
- renal tubular acidosis (usually subclinical)

## Investigation

- rheumatoid factor (RF) positive in nearly 100% of patients
- ANA positive in 70%
- anti-Ro (SSA) antibodies in 70% of patients with PSS
- anti-La (SSB) antibodies in 30% of patients with PSS
- Schirmer's test: filter paper near conjunctival sac to measure tear formation
- histology: focal lymphocytic infiltration
- also: hypergammaglobulinaemia, low C4

## Management

- artificial saliva and tears
- pilocarpine may stimulate saliva production

Which one of the following is most likely to indicate an underlying connective tissue disorder in a patient with Raynaud's phenomenon?

<input type="radio"/>	A. Chilblains
<input type="radio"/>	B. Bilateral symptoms
<input type="radio"/>	C. Female patient
<input type="radio"/>	D. Onset at 18 years old
<input type="radio"/>	E. Recurrent miscarriages

[Next question](#)

Raynaud's disease (i.e. primary) presents in young women with bilateral symptoms

A history of recurrent miscarriages could indicate systemic lupus erythematosus or anti-phospholipid syndrome. Chilblains (pernio) are itchy, painful purple swellings which occur on the fingers and toes after exposure to the cold. They are occasionally associated with underlying connective tissue disease but this is rare

### Raynaud's

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Factors suggesting underlying connective tissue disease

- onset after 40 years
- unilateral symptoms
- rashes
- presence of autoantibodies
- features which may suggest rheumatoid arthritis or SLE, for example arthritis or recurrent miscarriages
- digital ulcers, calcinosis
- very rarely: chilblains

Secondary causes

- connective tissue disorders: scleroderma (most common), rheumatoid arthritis, SLE
- leukaemia
- type I cryoglobulinaemia, cold agglutinins
- use of vibrating tools
- drugs: oral contraceptive pill, ergot
- cervical rib

## Management

- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months

A 33-year-old female is admitted to the Emergency Department due to right-sided weakness. She has a past history of deep vein thrombosis following the birth of her daughter. The only other past history of note is two miscarriages. A CT head confirms an ischaemic stroke in the left middle cerebral artery territory. What is the likely finding on echocardiography?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Normal                    |
| <input type="radio"/> | B. Dilated cardiomyopathy    |
| <input type="radio"/> | C. Bicuspid aortic valve     |
| <input type="radio"/> | D. Atrial septal defect      |
| <input type="radio"/> | E. Ventricular septal defect |

[Next question](#)

This is a typical MRCP question. On first sight this question appears to be pointing towards a paradoxical embolus. However, given the history of miscarriages and DVT a diagnosis of antiphospholipid syndrome is more likely.

### Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

#### Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

#### Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

## Management - based on BCSH guidelines

- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

A 35-year-old woman who has severe Raynaud's disease is reviewed in clinic. Three months ago she was started on nifedipine. Unfortunately this has had a minimal effect on her symptoms and has resulted in ankle oedema. What is the most appropriate next step in management?

<input type="radio"/>	A. Aspirin
<input type="radio"/>	B. Sympathectomy
<input type="radio"/>	C. Intravenous prostacyclin
<input type="radio"/>	D. Methotrexate
<input type="radio"/>	E. Intravenous infliximab

[Next question](#)

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- first-line: calcium channel blockers e.g. nifedipine
- IV prostacyclin infusions: effects may last several weeks/months



A 63-year-old man presents to the Emergency Department with a 2 day history of a painful and swollen left knee joint. Aspiration reveals positively birefringent crystals and no organisms are seen. Which of the following conditions are not recognised causes of the underlying condition?

<input type="radio"/>	A. Haemochromatosis
<input type="radio"/>	B. Low magnesium
<input type="radio"/>	C. High phosphate
<input type="radio"/>	D. Acromegaly
<input type="radio"/>	E. Hyperparathyroidism

[Next question](#)

A low phosphate predisposes to pseudogout

### Pseudogout

Pseudogout is a form of microcrystal synovitis caused by the deposition of calcium pyrophosphate dihydrate in the synovium

#### Risk factors

- hyperparathyroidism
- hypothyroidism
- haemochromatosis
- acromegaly
- low magnesium, low phosphate
- Wilson's disease

#### Features

- knee, wrist and shoulders most commonly affected
- joint aspiration: weakly-positively birefringent rhomboid shaped crystals
- x-ray: chondrocalcinosis

#### Management

- aspiration of joint fluid, to exclude septic arthritis
- NSAIDs or intra-articular, intra-muscular or oral steroids as for gout

A 23-year-old female presents with a painful ankle following an inversion injury whilst playing tennis. Which one of the following findings is least relevant when deciding whether an x-ray is needed?

<input type="radio"/>	A. Swelling immediately after the injury and now
<input type="radio"/>	B. Pain in the malleolar zone
<input type="radio"/>	C. Tenderness at the medial malleolar zone
<input type="radio"/>	D. Tenderness at the lateral malleolar zone
<input type="radio"/>	E. Cannot walk 4 steps immediately after the injury and now

[Next question](#)

### Ankle injury: Ottawa rules

The Ottawa Rules with for ankle x-rays have a sensitivity approaching 100%

An ankle x-ray is required only if there is any pain in the malleolar zone and any one of the following findings:

- bony tenderness at the lateral malleolar zone (from the tip of the lateral malleolus to include the lower 6 cm of posterior border of the fibula)
- bony tenderness at the medial malleolar zone (from the tip of the medial malleolus to the lower 6 cm of the posterior border of the tibia)
- inability to walk four weight bearing steps immediately after the injury and in the emergency department

There are also Ottawa rules available for both foot and knee injuries

A 28-year-old man is diagnosed with having ankylosing spondylitis. He presented with a six month history of back pain. On examination there is reduced lateral flexion of the spine but no evidence of any other complications. Which one of the following is the most likely to be offered as first-line treatment?

<input type="radio"/>	A. Exercise regime + NSAIDs
<input type="radio"/>	B. Exercise regime + infliximab
<input type="radio"/>	C. Physiotherapy + sulfasalazine
<input type="radio"/>	D. Physiotherapy + etanercept
<input type="radio"/>	E. Exercise regime + paracetamol

[Next question](#)

The anti-TNF drugs are currently only used for patients with severe ankylosing spondylitis which has failed to respond to NSAIDs.

### Ankylosing spondylitis: investigation and management

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

#### Investigation

Inflammatory markers (ESR, CRP) are typically raised although normal levels do not exclude ankylosing spondylitis.

HLA-B27 is of little use in making the diagnosis as it is positive in:

- 90% of patients with ankylosing spondylitis
- 10% of normal patients

Plain x-ray of the sacroiliac joints is the most useful investigation in establishing the diagnosis. Radiographs may be normal early in disease, later changes include:

- sacroilitis: subchondral erosions, sclerosis
- squaring of lumbar vertebrae
- 'bamboo spine' (late & uncommon)
- chest x-ray: apical fibrosis

Spirometry may show a restrictive defect due to a combination of pulmonary fibrosis, kyphosis and ankylosis of the costovertebral joints.

#### Management

Early diagnosis is now more important following the advent of anti-TNF therapy

- encourage regular exercise such as swimming
- NSAIDs
- physiotherapy
- the disease-modifying drugs which are used to treat rheumatoid arthritis (such as sulphasalazine) are only really useful if there is peripheral joint involvement
- TNF-alpha blockers such as etanercept and adalimumab are increasingly used. This approach for severe ankylosing spondylitis was supported by NICE in 2008

Which one of the following is most consistently associated with a poor prognosis in rheumatoid arthritis?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Anti-CCP antibodies |
| <input type="radio"/> | B. HLA DR2 allele      |
| <input type="radio"/> | C. Rapid onset         |
| <input type="radio"/> | D. Being a smoker      |
| <input type="radio"/> | E. Female sex          |

Next question

See below for further information on the effect of gender on prognosis.

### Rheumatoid arthritis: prognostic features

A number of features have been shown to predict a poor prognosis in patients with rheumatoid arthritis, as listed below

#### Poor prognostic features

- rheumatoid factor positive
- poor functional status at presentation
- HLA DR4
- X-ray: early erosions (e.g. after < 2 years)
- extra articular features e.g. nodules
- insidious onset
- anti-CCP antibodies

In terms of gender there seems to be a split in what the established sources state is associated with a poor prognosis. However both the American College of Rheumatology and the recent NICE guidelines (which looked at a huge number of prognosis studies) seem to conclude that female gender is associated with a poor prognosis.

**Question 109 of 118**

Next

You review a 40-year-old mechanic who presents with joint pains. For the past two months he has noticed intermittent pain, stiffness and swelling of the joints in his hands and feet. The stiffness tends to improve during the day but the pain tends to get worse. He has also noticed stiffness in his back but cannot remember any aggravating injury. You order some blood tests (taken during an acute attack) which are reported as follows:

Rheumatoid factor	Negative
Anti-cyclic citrullinated peptide antibody	Positive
Uric acid	0.3 mmol/l (0.18 - 0.48)
ESR	41 mm/hr

What is the most likely diagnosis?

- ☐ A. Reactive arthritis
- ☐ B. Ankylosing spondylitis
- ☐ C. Gout
- ☐ D. Osteoarthritis
- ☐ E. Rheumatoid arthritis

Next question

Anti-cyclic citrullinated peptide antibodies are associated with rheumatoid arthritis

Anti-cyclic citrullinated peptide antibody is highly specific for rheumatoid arthritis.

**Rheumatoid factor**

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG

RF can be detected by either

- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:

- Sjogren's syndrome (around 100%)

- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy

A 30-year-old female who is known to have antiphospholipid syndrome is diagnosed as having a deep vein thrombosis. This is her first thrombotic event. How should her anticoagulation be managed?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Life-long low-dose aspirin   |
| <input type="radio"/> | B. 6 months warfarin, target INR 2 - 3  |
| <input type="radio"/> | C. Life-long warfarin, target INR 3 - 4   |
| <input type="radio"/> | D. Life-long warfarin, target INR 2 - 3   |
| <input type="radio"/> | E. 6 months warfarin, target INR 2 - 3 followed by life-long low-dose aspirin and clopidogrel |

Next question

This is a tough question and some textbooks may contradict this answer, suggesting either lifelong warfarin or a target INR of 3-4. Please see the link to the BCSH guidelines. There is also a recent review in JAMA 2006; 295(9): 1050-7

### Antiphospholipid syndrome

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

A key point for the exam is to appreciate that antiphospholipid syndrome causes a paradoxical rise in the APTT. This is due to an ex-vivo reaction of the lupus anticoagulant autoantibodies with phospholipids involved in the coagulation cascade

#### Features

- venous/arterial thrombosis
- recurrent fetal loss
- livedo reticularis
- thrombocytopenia
- prolonged APTT
- other features: pre-eclampsia, pulmonary hypertension

#### Associations other than SLE

- other autoimmune disorders
- lymphoproliferative disorders
- phenothiazines (rare)

Management - based on BCSH guidelines



- initial venous thromboembolic events: evidence currently supports use of warfarin with a target INR of 2-3 for 6 months
- recurrent venous thromboembolic events: lifelong warfarin; if occurred whilst taking warfarin then increase target INR to 3-4
- arterial thrombosis should be treated with lifelong warfarin with target INR 2-3

**Question 111 of 118**

Next

A 20-year-old woman is reviewed in the rheumatology clinic. She has been referred due to a three month history of arthralgia, lethargy, muscle pains and Raynaud's phenomenon. On examination she is noted to have slightly swollen hands but no significant synovitis. A number of blood tests are ordered:

Hb	12.9 g/dl
Platelets	$282 \times 10^9/l$
WBC	$6.2 \times 10^9/l$

Rheumatoid factor	Negative
ANA	Positive
Anti-dsDNA antibodies	Negative
CRP	25 mg/l
ESR	39 mm/hr
Creatine kinase	675 ng/mL (50-200)

Given the likely diagnosis, which other antibodies are most likely to be present?

- ☐ A. Anti-Scl-70
- ☐ B. Anti-centromere
- ☐ C. Anti-Jo
- ☐ D. Anti-RO
- ☐ E. Anti-RNP

Next question

Anti-ribonuclear protein (anti-RNP) = mixed connective tissue disease

This patient has typical features of mixed connective tissue disease (e.g. arthralgia, myositis and Raynaud's). To confirm the diagnosis anti-RNP antibodies need to be detected.

**Mixed connective tissue disease**

Features of SLE, systemic sclerosis and polymyositis

Anti-RNP positive

Next

### Question 112 of 118

A 62-year-old man with lung cancer is suspected of having dermatomyositis. Which one of the following antibodies is most likely to be positive?

<input type="radio"/>	A. Anti-nuclear antibodies
<input type="radio"/>	B. Anti-centromere bodies
<input type="radio"/>	C. Anti-scl-70 antibodies
<input type="radio"/>	D. Anti-Jo-1 antibodies
<input type="radio"/>	E. Anti-Mi-2 antibodies

[Next question](#)

Dermatomyositis antibodies: ANA most common, anti-Mi-2 most specific

### Dermatomyositis: investigations and management

#### Investigations

- elevated creatine kinase
- EMG
- muscle biopsy
- ANA positive in 60%
- anti-Jo-1 antibodies are not commonly seen in dermatomyositis - they are more common in polymyositis where they are seen in a pattern of disease associated with lung involvement, Raynaud's and fever
- anti-Mi-2 antibodies are highly specific for dermatomyositis, but are only seen in around 25% of patients

#### Management

- prednisolone

A 50-year-old woman complains of pain in her right elbow. This has been present for the past four weeks and is maximal around 4-5cm distal from the lateral aspect of the elbow joint. The pain is made worse by extending the elbow and pronating the forearm. What is the most likely diagnosis?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. Lateral epicondylitis       |
| <input type="radio"/> | B. Radial tunnel syndrome      |
| <input type="radio"/> | C. De Quervain's tenosynovitis |
| <input type="radio"/> | D. Cubital tunnel syndrome     |
| <input type="radio"/> | E. Medial epicondylitis        |

[Next question](#)

### Elbow pain

The table below details some of the characteristic features of conditions causing elbow pain:

<b>Lateral epicondylitis (tennis elbow)</b>	<p>Features</p> <ul style="list-style-type: none"> <li>• pain and tenderness localised to the lateral epicondyle</li> <li>• pain worse on resisted wrist extension with the elbow extended or supination of the forearm with the elbow extended</li> <li>• episodes typically last between 6 months and 2 years. Patients tend to have acute pain for 6-12 weeks</li> </ul>
<b>Medial epicondylitis (golfer's elbow)</b>	<p>Features</p> <ul style="list-style-type: none"> <li>• pain and tenderness localised to the medial epicondyle</li> <li>• pain is aggravated by wrist flexion and pronation</li> <li>• symptoms may be accompanied by numbness / tingling in the 4th and 5th finger due to ulnar nerve involvement</li> </ul>
<b>Radial tunnel syndrome</b>	<p>Most commonly due to compression of the posterior interosseous branch of the radial nerve. It is thought to be a result of overuse.</p> <p>Features</p> <ul style="list-style-type: none"> <li>• symptoms are similar to lateral epicondylitis making it difficult to diagnose</li> <li>• however, the pain tends to be around 4-5 cm distal to the lateral epicondyle</li> <li>• symptoms may be worsened by extending the elbow and pronating the forearm</li> </ul>
<b>Cubital tunnel syndrome</b>	<p>Due to the compression of the ulnar nerve.</p> <p>Features</p> <ul style="list-style-type: none"> <li>• initially intermittent tingling in the 4th and 5th finger</li> <li>• may be worse when the elbow is resting on a firm surface or flexed for extended periods</li> <li>• later numbness in the 4th and 5th finger with associated weakness</li> </ul>
<b>Olecranon bursitis</b>	<p>Swelling over the posterior aspect of the elbow. There may be associated pain, warmth and erythema. It typically affects middle-aged male patients.</p>

**Question 114 of 118**

Next

Which one of the following antibodies is most specific for systemic lupus erythematosus?

<input type="radio"/>	A. Anti-neutrophil cytoplasmic antibodies
<input type="radio"/>	B. Anti-nuclear antibodies
<input type="radio"/>	C. Anti-Sm antibodies
<input type="radio"/>	D. Anti-RNP antibodies
<input type="radio"/>	E. Anti-cardiolipin antibodies

Next question

SLE: ANA is 99% sensitive - anti-Sm & anti-dsDNA are 99% specific

**SLE: investigations**

## Immunology

- 99% are ANA positive
- 20% are rheumatoid factor positive
- anti-dsDNA: highly specific (> 99%), but less sensitive (70%)
- anti-Smith: most specific (> 99%), sensitivity (30%)

## Monitoring

- ESR: during active disease the CRP is characteristically normal - a raised CRP may indicate underlying infection
- complement levels (C3, C4) are low during active disease (formation of complexes leads to consumption of complement)
- anti-dsDNA titres can be used for disease monitoring (but note not present in all patients)

Which one of the following is most recognised as a potential complication in a patient with ankylosing spondylitis?

<input type="radio"/>	A. Heart block
<input type="radio"/>	B. Aortic stenosis
<input type="radio"/>	C. Achalasia
<input type="radio"/>	D. Diabetes mellitus
<input type="radio"/>	E. Bronchiectasis

[Next question](#)

#### Ankylosing spondylitis features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis

#### Ankylosing spondylitis: features

Ankylosing spondylitis is a HLA-B27 associated spondyloarthropathy. It typically presents in males (sex ratio 5:1) aged 20-30 years old.

#### Features

- typically a young man who presents with lower back pain and stiffness of insidious onset
- stiffness is usually worse in the morning and improves with exercise
- the patient may experience pain at night which improves on getting up

#### Clinical examination

- reduced lateral flexion
- reduced forward flexion - Schober's test - a line is drawn 10 cm above and 5 cm below the back dimples (dimples of Venus). The distance between the two lines should increase by more than 5 cm when the patient bends as far forward as possible
- reduced chest expansion

## Other features - the 'A's

- Apical fibrosis
- Anterior uveitis
- Aortic regurgitation
- Achilles tendonitis
- AV node block
- Amyloidosis
- and cauda equina syndrome
- peripheral arthritis (25%, more common if female)

A 58-year-old woman with a history of left hip osteoarthritis presents for review. She is currently taking co-codamol 30/500 for pain on a regular basis but this is unfortunately not controlling her symptoms. There is no past medical history of note, in particular no asthma or gastrointestinal problems. What is the most suitable next step in management?

- ☐ A. Switch to regular oral tramadol
- ☐ B. Add topical ibuprofen
- ☐ C. Add oral diclofenac + proton pump inhibitor
- ☐ D. Add oral etoricoxib
- ☐ E. Add oral diclofenac

[Next question](#)

NICE recommend co-prescribing a PPI with NSAIDs in all patients with osteoarthritis

Topical NSAIDs are only indicated for osteoarthritis of the knee or hand.

### Osteoarthritis: management

NICE published guidelines on the management of osteoarthritis (OA) in 2008

- all patients should be offered help with weight loss, given advice about local muscle strengthening exercises and general aerobic fitness
- paracetamol and topical NSAIDs are first-line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand
- second-line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream and intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed with NSAIDs and COX-2 inhibitors. These drugs should be avoided if the patient takes aspirin
- non-pharmacological treatment options include supports and braces, TENS and shock absorbing insoles or shoes
- if conservative methods fail then refer for consideration of joint replacement

What is the role of glucosamine?

- normal constituent of glycosaminoglycans in cartilage and synovial fluid
- a systematic review of several double blind RCTs of glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrowing and improved pain scores
- more recent studies have however been mixed
- the 2008 NICE guidelines suggest it is not recommended



- a 2008 Drug and Therapeutics Bulletin review advised that whilst glucosamine provides modest pain relief in knee osteoarthritis it should not be prescribed on the NHS due to limited evidence of cost-effectiveness

Which one of the following is least associated with the development of gout?

<input type="radio"/>	A. Psoriasis
<input type="radio"/>	B. Lesch-Nyhan syndrome
<input type="radio"/>	C. Lymphoma
<input type="radio"/>	D. Lithium toxicity
<input type="radio"/>	E. Renal failure

Next question

### Gout: predisposing factors

Gout is a form of microcrystal synovitis caused by the deposition of monosodium urate monohydrate in the synovium. It is caused by chronic hyperuricaemia (uric acid > 0.45 mmol/l)

Decreased excretion of uric acid

- drugs\*: diuretics
- chronic kidney disease
- lead toxicity

Increased production of uric acid

- myeloproliferative/lymphoproliferative disorder
- cytotoxic drugs
- severe psoriasis

Lesch-Nyhan syndrome

- hypoxanthine-guanine phosphoribosyl transferase deficiency
- inheritance = x-linked recessive
- features: gout, renal failure, learning difficulties, head-banging

\*aspirin in a dose of 75-150mg is not thought to have a significant effect on plasma urate levels - the British Society for Rheumatology recommend it should be continued if required for cardiovascular prophylaxis

### Question 118 of 118

A 44-year-old woman is seen in the rheumatology clinic. She has been referred with Raynaud's phenomenon. During the review of systems she mentions that her GP is organising an endoscopy to investigate dyspepsia. On examination she is noted to have tight, shiny skin over her fingers. Which one of the following complications she most likely to develop?

<input type="radio"/>	A. Bronchiectasis
<input type="radio"/>	B. Angiodysplasia
<input type="radio"/>	C. Arterial hypertension
<input type="radio"/>	D. Chronic kidney disease
<input type="radio"/>	E. Pulmonary hypertension

This patient is likely to have CREST syndrome. Unfortunately pulmonary hypertension is one of the more common late complications seen in such patients.

### Systemic sclerosis

Systemic sclerosis is a condition of unknown aetiology characterised by hardened, sclerotic skin and other connective tissues. It is four times more common in females

There are three patterns of disease:

#### Limited cutaneous systemic sclerosis

- Raynaud's may be first sign
- scleroderma affects face and distal limbs predominately
- associated with anti-centromere antibodies
- a subtype of limited systemic sclerosis is CREST syndrome: Calcinosis, Raynaud's phenomenon, oEsophageal dysmotility, Sclerodactyly, Telangiectasia

#### Diffuse cutaneous systemic sclerosis

- scleroderma affects trunk and proximal limbs predominately
- associated with scl-70 antibodies
- hypertension, lung fibrosis and renal involvement seen
- poor prognosis

#### Scleroderma (without internal organ involvement)

- tightening and fibrosis of skin
- may be manifest as plaques (morphoea) or linear

## Antibodies

- ANA positive in 90%
- RF positive in 30%
- anti-scl-70 antibodies associated with diffuse cutaneous systemic sclerosis
- anti-centromere antibodies associated with limited cutaneous systemic sclerosis

**Question 1 of 93**

Next

A 27-year-old man is investigated for haemoptysis. He is a non-smoker and has no respiratory history of note. Whilst awaiting a bronchoscopy he becomes lethargic and anorexic. Blood tests show the following:

Na <sup>+</sup>	141 mmol/l
K <sup>+</sup>	5.3 mmol/l
Urea	16.7 mmol/l
Creatinine	271 µmol/l

A renal biopsy is performed and shows linear IgG deposits along the basement membrane.

What type of antibodies are most likely to cause this type of presentation?

- ☐ A. cANCA
- ☐ B. IgA
- ☐ C. pANCA
- ☐ D. Anti-nuclear antibodies (ANA)
- ☐ E. Anti-glomerular basement membrane (anti-GBM) antibodies

Next question

**Goodpasture's syndrome**

- IgG deposits on renal biopsy
- anti-GBM antibodies

The combination of haemoptysis, renal failure and linear IgG deposits points to a diagnosis of Goodpasture's syndrome.

The ANCA-related nephropathies are associated with crescentic glomerulonephritis.

**Goodpasture's syndrome**

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Goodpasture's syndrome is more common in men (sex ratio 2:1) and has a bimodal age distribution (peaks in 20-30 and 60-70 age bracket). It is associated with HLA DR2.

## Features

- pulmonary haemorrhage
- followed by rapidly progressive glomerulonephritis

## Factors which increase likelihood of pulmonary haemorrhage

- smoking
- lower respiratory tract infection
- pulmonary oedema
- inhalation of hydrocarbons
- young males

## Investigations

- renal biopsy: linear IgG deposits along basement membrane
- raised transfer factor secondary to pulmonary haemorrhages

## Management

- plasma exchange
- steroids
- cyclophosphamide

## Question 2 of 93

Next

A 24-year-old woman is diagnosed as having nephrotic syndrome after being investigated for proteinuria. A diagnosis of minimal change glomerulonephritis is made. What is the most appropriate initial treatment to reduce proteinuria?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Protein restriction in diet             |
| <input type="radio"/> | B. No treatment shown to effective         |
| <input type="radio"/> | C. Angiotensin-converting-enzyme inhibitor |
| <input type="radio"/> | D. Diuretic                                |
| <input type="radio"/> | E. Prednisolone                            |

Next question

Minimal change glomerulonephritis - prednisolone

Angiotensin-converting-enzyme inhibitors may be used to reduce proteinuria in patients with heavy proteinuria or who have a slow response to prednisolone

### Minimal change glomerulonephritis

Minimal change glomerulonephritis nearly always presents as nephrotic syndrome, accounting for 75% of cases in children and 25% in adults

The majority of cases are idiopathic, but in around 10-20% a cause is found:

- drugs: NSAIDs, rifampicin
- Hodgkin's lymphoma, thymoma
- infectious mononucleosis

### Features

- nephrotic syndrome
- normotension - hypertension is rare
- highly selective proteinuria\*
- renal biopsy: electron microscopy shows fusion of podocytes

### Management

- majority of cases (80%) are steroid responsive
- cyclophosphamide is the next step for steroid resistant cases

Prognosis is overall good, although relapse is common. Roughly:

- 1/3 have just one episode
- 1/3 have infrequent relapses
- 1/3 have frequent relapses which stop before adulthood

\*only intermediate-sized proteins such as albumin and transferrin leak through the glomerulus



### Question 3 of 93

Next

A 64-year-old female is brought to the Emergency Department by her family, who are concerned about her increasing confusion over the past 2 days. On examination she is found to be pyrexial at 38°C. Blood tests reveal:

Hb	9.6 g/dl
Platelets	$65 \times 10^9/l$
WCC	$11.1 \times 10^9/l$
Urea	23.1 mmol/l
Creatinine	366 $\mu$ mol/l

What is the most likely diagnosis?

- ☐ A. Wegener's granulomatosis
- ☐ B. Thrombotic thrombocytopenic purpura
- ☐ C. Haemolytic uraemic syndrome
- ☐ D. Idiopathic thrombocytopenic purpura
- ☐ E. Rapidly progressive glomerulonephritis

Next question

HUS or TTP? Neuro signs and purpura point towards TTP

The combination of neurological features, renal failure, pyrexia and thrombocytopenia point towards a diagnosis of thrombotic thrombocytopenic purpura

#### Thrombotic thrombocytopenic purpura

Pathogenesis of thrombotic thrombocytopenic purpura (TTP)

- abnormally large and sticky multimers of von Willebrand's factor cause platelets to clump within vessels
- in TTP there is a deficiency of caspase which breakdowns large multimers of von Willebrand's factor
- overlaps with haemolytic uraemic syndrome (HUS)

Features

- rare, typically adult females
- fever
- fluctuating neuro signs (microemboli)
- microangiopathic haemolytic anaemia
- thrombocytopenia

- renal failure

## Causes

- post-infection e.g. urinary, gastrointestinal
- pregnancy
- drugs: ciclosporin, oral contraceptive pill, penicillin, clopidogrel, aciclovir
- tumours
- SLE
- HIV

**Question 4 of 93**

Next

A 45-year-old female with nephrotic syndrome develops renal vein thrombosis. What changes in patients with nephrotic syndrome predispose to the development of venous thromboembolism?

<input type="radio"/>	A. Reduced excretion of protein S
<input checked="" type="radio"/>	B. Loss of antithrombin III
<input type="radio"/>	C. Reduced excretion of protein C
<input type="radio"/>	D. Loss of fibrinogen
<input type="radio"/>	E. Reduced metabolism of vitamin K

Next question

**Nephrotic syndrome**

Triad of:

- 1. Proteinuria (> 3g/24hr) causing
- 2. Hypoalbuminaemia (< 30g/L) and
- 3. Oedema

Loss of antithrombin-III, proteins C and S and an associated rise in fibrinogen levels predispose to thrombosis. Loss of thyroxine-binding globulin lowers the total, but not free, thyroxine levels.

**Question 5 of 93**

Next

A 14-year-old girl is referred to the paediatric unit with reduced urine output and lethargy. She has been passing bloody diarrhoea for the past four days. On admission she appears dehydrated. Bloods show the following:

Na <sup>+</sup>	142 mmol/l
K <sup>+</sup>	4.8 mmol/l
Bicarbonate	22 mmol/l
Urea	10.1 mmol/l
Creatinine	176 µmol/l
Hb	10.4 g/dl
MCV	90 fl
Plt	91 * 10 <sup>9</sup> /l
WBC	14.4 * 10 <sup>9</sup> /l

Given the likely diagnosis, which one of the following organisms is the most likely cause?

- ☐ A. *Campylobacter*
- ☐ B. Giardiasis
- ☐ C. *E. coli*
- ☐ D. *Salmonella*
- ☐ E. *Shigella*

Next question

Haemolytic uraemic syndrome - classically caused by E coli O157:H7

**Haemolytic uraemic syndrome**

Haemolytic uraemic syndrome is generally seen in young children and produces a triad of:

- acute renal failure
- microangiopathic haemolytic anaemia
- thrombocytopenia

**Causes**

- post-dysentery - classically E coli O157:H7 ('verotoxigenic', 'enterohaemorrhagic')
- tumours

- pregnancy
- ciclosporin, the Pill
- systemic lupus erythematosus
- HIV

### Investigations

- full blood count: anaemia, thrombocytopaenia, fragmented blood film
- U&E: acute renal failure
- stool culture

### Management

- treatment is supportive e.g. Fluids, blood transfusion and dialysis if required
- there is no role for antibiotics, despite the preceding diarrhoeal illness in many patients
- the indications for plasma exchange in HUS are complicated. As a general rule plasma exchange is reserved for severe cases of HUS not associated with diarrhoea

### Question 6 of 93

Next

A 17-year-old man is referred to the local nephrology unit for investigation. He reports having several episodes of visible haematuria. There is no history of abdominal or loin pain. These typically seem to occur within a day or two of developing an upper respiratory tract infection. Urine dipstick is normal. Blood tests show the following:

Na <sup>+</sup>	141 mmol/l
K <sup>+</sup>	4.3 mmol/l
Bicarbonate	25 mmol/l
Urea	4.1 mmol/l
Creatinine	72 µmol/l

What is the most likely diagnosis?

- ☐ A. *Chlamydia*
- ☐ B. Bladder cancer
- ☐ C. IgA nephropathy
- ☐ D. Rhinovirus-associated nephropathy
- ☐ E. Post-streptococcal glomerulonephritis

Next question

## IgA nephropathy

### Basics

- also called Berger's disease or mesangioproliferative glomerulonephritis
- commonest cause of glomerulonephritis worldwide
- pathogenesis unknown, ?mesangial deposition of IgA immune complexes
- histology: mesangial hypercellularity, positive immunofluorescence for IgA & C3

### Differentiating between IgA nephropathy and post-streptococcal glomerulonephritis

- post-streptococcal glomerulonephritis is associated with low complement levels
- main symptom in post-streptococcal glomerulonephritis is proteinuria (although haematuria can occur)
- there is typically an interval between URTI and the onset of renal problems in post-streptococcal glomerulonephritis

### Presentations

- young male, recurrent episodes of macroscopic haematuria

- typically associated with mucosal infections e.g., URTI
- nephrotic range proteinuria is rare
- renal failure

#### Associated conditions

- alcoholic cirrhosis
- coeliac disease/dermatitis herpetiformis

#### Management

- steroids/immunosuppressants not be shown to be useful

#### Prognosis

- 25% of patients develop ESRF
- markers of good prognosis: frank haematuria
- markers of poor prognosis: male gender, proteinuria (especially > 2 g/day), hypertension, smoking, hyperlipidaemia, ACE genotype DD

**Question 7 of 93**

Next

A 54-year-old woman with a history of membranous glomerulonephritis secondary to systemic lupus erythematosus is admitted to hospital. Her previous stable renal function has deteriorated rapidly. The following blood tests were obtained:

Na <sup>+</sup>	139 mmol/l
K <sup>+</sup>	5.8 mmol/l
Urea	44 mmol/l
Creatinine	867 µmol/l
Albumin	17 g/l
ESR	49 mm/hr
Urinary protein	14 g/24 hours
Urine dipstick	protein +++ blood ++

What has likely caused the sudden deterioration in renal function?

- ☐ A. Exacerbation of SLE
- ☐ B. Renal vein thrombosis
- ☐ C. Bilateral hydronephrosis
- ☐ D. Acute interstitial nephritis
- ☐ E. Analgesic nephropathy

Next question

Nephrotic syndrome predisposes to thrombotic episodes, possibly due to loss of antithrombin III. These commonly occur in the renal veins and may be bilateral. Common symptoms include loin pain and haematuria.

A greater rise in the ESR would be expected if the renal failure was due to an exacerbation of SLE.

**Nephrotic syndrome: complications****Complications**

- increased risk of infection due to urinary immunoglobulin loss
- increased risk of thromboembolism related to loss of antithrombin III and plasminogen in the urine
- hyperlipidaemia
- hypocalcaemia (vitamin D and binding protein lost in urine)
- acute renal failure



## Question 8 of 93

Next

A 25-year-old man has a renal biopsy due to worsening renal function. This reveals linear IgG deposits along the basement membrane. What is the most likely diagnosis?

<input type="radio"/>	A. Systemic lupus erythematosus
<input type="radio"/>	B. IgA nephropathy
<input type="radio"/>	C. Minimal change disease
<input type="radio"/>	D. Post-streptococcal glomerulonephritis
<input type="radio"/>	E. Goodpasture's syndrome

Next question

### Goodpasture's syndrome

- IgG deposits on renal biopsy
- anti-GBM antibodies

These changes are characteristic of Goodpasture's syndrome.

### Goodpasture's syndrome

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Goodpasture's syndrome is more common in men (sex ratio 2:1) and has a bimodal age distribution (peaks in 20-30 and 60-70 age bracket). It is associated with HLA DR2.

#### Features

- pulmonary haemorrhage
- followed by rapidly progressive glomerulonephritis

#### Factors which increase likelihood of pulmonary haemorrhage

- smoking
- lower respiratory tract infection
- pulmonary oedema
- inhalation of hydrocarbons
- young males

#### Investigations

- renal biopsy: linear IgG deposits along basement membrane
- raised transfer factor secondary to pulmonary haemorrhages

## Management

- plasma exchange
- steroids
- cyclophosphamide

**Question 9 of 93**

Next

A 65-year-old female with a 20 year history of rheumatoid arthritis is referred to the acute medical unit with bilateral leg oedema. The following results are obtained:

Urea	11.2 mmol/l
Creatinine	205 µmol/l
Albumin	26 g/l
Bilirubin	12 mmol/l
ALP	120 IU/l
Urine protein	6.2 g/24 hours

Which investigation is most likely to lead to the correct diagnosis?

- ☐ A. CT abdomen
- ☐ B. Plasma magnesium
- ☐ C. Intravenous urogram
- ☐ D. Rectal biopsy
- ☐ E. Renal angiogram

Next question

This rather odd question fooled most candidates when it appeared. The chronic inflammatory process (rheumatoid) predisposes to amyloidosis which in turn can cause nephrotic syndrome. Rectal biopsy is an (infrequent) test done to look for amyloidosis.

Rheumatoid drugs such as gold may cause nephrotic syndrome but none of the other options point to this as an answer

**Amyloidosis: types****AL amyloid**

- L for immunoglobulin Light chain fragment
- due to myeloma, Waldenstrom's, MGUS
- features include: cardiac and neurological involvement, macroglossia, periorbital ecchymoses

**AA amyloid**

- A for precursor serum amyloid A protein, an acute phase reactant
- seen in chronic infection/inflammation eg. TB, Bronchiectasis, Rheumatoid Arthritis

- features: renal involvement most common feature

#### Beta-2 microglobulin amyloidosis

- precursor protein is beta-2 microglobulin, part of the major histocompatibility complex
- associated with patients on renal dialysis

**Question 10 of 93**

Next

Which one of the following types of glomerulonephritis is most characteristically associated with partial lipodystrophy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Minimal change disease                   |
| <input type="radio"/> | B. Diffuse proliferative glomerulonephritis |
| <input type="radio"/> | C. Mesangiocapillary glomerulonephritis     |
| <input type="radio"/> | D. Membranous glomerulonephritis            |
| <input type="radio"/> | E. Rapidly progressive glomerulonephritis   |

Next question

**Mesangiocapillary glomerulonephritis (membranoproliferative)**

- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

Type 2 mesangiocapillary glomerulonephritis is associated with partial lipodystrophy. Type 1 is seen in association with hepatitis C and cryoglobulinaemia

Mesangiocapillary glomerulonephritis is sometimes referred to as membranoproliferative glomerulonephritis

**Glomerulonephritides**

Knowing a few key facts is the best way to approach the difficult subject of glomerulonephritis:

**Membranous glomerulonephritis**

- presentation: proteinuria / nephrotic syndrome / chronic kidney disease
- cause: infections, rheumatoid drugs, malignancy
- 1/3 resolve, 1/3 respond to cytotoxics, 1/3 develop chronic kidney disease

IgA nephropathy - aka Berger's disease, mesangioproliferative GN

- typically young adult with haematuria following an URTI

**Diffuse proliferative glomerulonephritis**

- classical post-streptococcal glomerulonephritis in child
- presents as nephritic syndrome / acute kidney injury
- most common form of renal disease in SLE

### Minimal change disease

- typically a child with nephrotic syndrome (accounts for 80%)
- causes: Hodgkin's, NSAIDs
- good response to steroids

### Focal segmental glomerulosclerosis

- may be idiopathic or secondary to HIV, heroin
- presentation: proteinuria / nephrotic syndrome / chronic kidney disease

### Rapidly progressive glomerulonephritis - aka crescentic glomerulonephritis

- rapid onset, often presenting as acute kidney injury
- causes include Goodpasture's, ANCA positive vasculitis

### Mesangiocapillary glomerulonephritis (membranoproliferative)

- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

**Question 11 of 93**

Next

A 67-year-old woman presents for review due to ankle swelling. She has a history of rheumatoid arthritis which was diagnosed when she was 24 years old and a 8 year history of type 2 diabetes mellitus. Her current medication includes metformin and methotrexate. On examination she has bilateral pitting lower limb oedema. A 24 hour urine collection is reported as follows:

24 hr urinary protein	4.8g
-----------------------	------

What is the most likely cause of her leg oedema?

- |                                  |  |
|----------------------------------|--|
| <input type="radio"/>            | A. Diabetic nephropathy                              |
| <input type="radio"/>            | B. Nephrotic syndrome secondary to methotrexate      |
| <input type="radio"/>            | C. Dilated cardiomyopathy secondary to methotrexate  |
| <input checked="" type="radio"/> | D. Amyloidosis                                       |
| <input type="radio"/>            | E. Protein-losing enteropathy secondary to metformin |

Next question

This patient has developed nephrotic syndrome secondary to amyloidosis, a recognised complication of inflammatory conditions such as rheumatoid arthritis. Methotrexate is not a common cause of nephrotic syndrome. Diabetic nephropathy often presents as nephrotic syndrome but typically develops at least 15 years after onset.

**Nephrotic syndrome: causes**

Primary glomerulonephritis accounts for around 80% of cases

- minimal change glomerulonephritis (causes 80% in children, 30% in adults)
- membranous glomerulonephritis
- focal segmental glomerulosclerosis
- membranoproliferative glomerulonephritis

Systemic disease (about 20%)

- diabetes mellitus
- systemic lupus erythematosus
- amyloidosis

Drugs

- gold (sodium aurothiomalate), penicillamine

## Others

- congenital
- neoplasia: carcinoma, lymphoma, leukaemia, myeloma
- infection: bacterial endocarditis, hepatitis B, malaria



A sample of tissue from a renal biopsy is viewed using an electron microscope. Podocyte fusion is seen. Which one of the following types of glomerulonephritis is most associated with this finding?

<input type="radio"/>	A. Membranous glomerulonephritis
<input type="radio"/>	B. IgA nephropathy
<input type="radio"/>	C. Focal segmental glomerulosclerosis
<input type="radio"/>	D. Mesangiocapillary glomerulonephritis
<input type="radio"/>	E. Minimal change glomerulonephritis

[Next question](#)

Podocyte fusion is seen in minimal change glomerulonephritis but may occasionally be a feature of focal segmental glomerulosclerosis as well. Minimal change glomerulonephritis however is far more common

### Minimal change glomerulonephritis

Minimal change glomerulonephritis nearly always presents as nephrotic syndrome, accounting for 75% of cases in children and 25% in adults

The majority of cases are idiopathic, but in around 10-20% a cause is found:

- drugs: NSAIDs, rifampicin
- Hodgkin's lymphoma, thymoma
- infectious mononucleosis

### Features

- nephrotic syndrome
- normotension - hypertension is rare
- highly selective proteinuria\*
- renal biopsy: electron microscopy shows fusion of podocytes

### Management

- majority of cases (80%) are steroid responsive
- cyclophosphamide is the next step for steroid resistant cases

Prognosis is overall good, although relapse is common. Roughly:

- 1/3 have just one episode
- 1/3 have infrequent relapses
- 1/3 have frequent relapses which stop before adulthood

\*only intermediate-sized proteins such as albumin and transferrin leak through the glomerulus

### Question 13 of 93

Next

A 54-year-old man who had a renal transplant two years ago is reviewed in clinic. He is currently taking a combination of ciclosporin and mycophenolate as immunosuppressive therapy. Two weeks ago he was discharged on oral fluconazole after inpatient treatment for a fungal pneumonia. His creatinine level has increased from 114  $\mu\text{mol/l}$  before hospital admission to 187  $\mu\text{mol/l}$  today. What is the most likely factor contributing to this rise?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Amphotericin-B induced membranous glomerulonephritis       |
| <input type="radio"/> | B. Ciclosporin nephrotoxicity                                 |
| <input type="radio"/> | C. 5-fluorocytosine induced minimal change glomerulonephritis |
| <input type="radio"/> | D. Mycophenolate nephrotoxicity                               |
| <input type="radio"/> | E. Fluconazole nephrotoxicity                                 |

Next question

Fluconazole inhibits the metabolism of ciclosporin which increases the risk of ciclosporin nephrotoxicity.

### Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphatase that activates various transcription factors in T cells

Adverse effects of ciclosporin (note how everything is increased - fluid, BP,  $\text{K}^+$ , hair, gums, glucose)

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- gingival hyperplasia
- tremor
- impaired glucose tolerance

Interestingly for an immunosuppressant, ciclosporin is noted by the BNF to be 'virtually non-myelotoxic'.

### Indications

- following organ transplantation
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- ulcerative colitis
- pure red cell aplasia

Each of the following is a risk factor for renal stone formation, except:

<input type="radio"/>	A. Renal tubular acidosis
<input type="radio"/>	B. Cadmium
<input type="radio"/>	C. Hyperparathyroidism
<input type="radio"/>	D. Dehydration
<input type="radio"/>	E. Cystinosis

Next question

Cystinuria, not cystinosis, is a risk factor for renal stone formation

### Renal stones: risk factors

#### Risk factors

- dehydration
- hypercalciuria, hyperparathyroidism, hypercalcaemia
- cystinuria
- high dietary oxalate
- renal tubular acidosis
- medullary sponge kidney, polycystic kidney disease
- beryllium or cadmium exposure

#### Risk factors for urate stones

- gout
- ileostomy: loss of bicarbonate and fluid results in acidic urine, causing the precipitation of uric acid

#### Drug causes

- drugs that promote calcium stones: loop diuretics, steroids, acetazolamide, theophylline
- thiazides can prevent calcium stones (increase distal tubular calcium resorption)

Each one of the following is a recognised side-effect of erythropoietin, except:

<input type="radio"/>	A. Urticaria
<input type="radio"/>	B. Hypertension
<input type="radio"/>	C. Bone aches
<input type="radio"/>	D. Long bone fractures
<input type="radio"/>	E. Pure red cell aplasia

Next question

## Erythropoietin

Erythropoietin is a haematopoietic growth factor that stimulates the production of erythrocytes. The main uses of erythropoietin are to treat the anaemia associated with chronic kidney disease and that associated with cytotoxic therapy.

Side-effects of erythropoietin

- accelerated hypertension potentially leading to encephalopathy and seizures (blood pressure increases in 25% of patients)
- bone aches
- flu-like symptoms
- skin rashes, urticaria
- pure red cell aplasia\* (due to antibodies against erythropoietin)
- raised PCV increases risk of thrombosis (e.g. Fistula)
- iron deficiency 2nd to increased erythropoiesis

There are a number of reasons why patients may fail to respond to erythropoietin therapy:

- iron deficiency
- inadequate dose
- concurrent infection/inflammation
- hyperparathyroid bone disease
- aluminium toxicity

\*the risk is greatly reduced with darbepoetin

A 27-year-old man is diagnosed with Goodpasture's syndrome. Which one of the following does not increase the likelihood of a pulmonary haemorrhage?

<input type="radio"/>	A. Smoking
<input type="radio"/>	B. Inhalation of hydrocarbons
<input type="radio"/>	C. Male gender
<input type="radio"/>	D. Dehydration
<input type="radio"/>	E. Lower respiratory tract infection

Dehydration may decrease the likelihood of a pulmonary haemorrhage. Pulmonary oedema is associated with an increased risk

### Goodpasture's syndrome

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Goodpasture's syndrome is more common in men (sex ratio 2:1) and has a bimodal age distribution (peaks in 20-30 and 60-70 age bracket). It is associated with HLA DR2.

#### Features

- pulmonary haemorrhage
- followed by rapidly progressive glomerulonephritis

#### Factors which increase likelihood of pulmonary haemorrhage

- smoking
- lower respiratory tract infection
- pulmonary oedema
- inhalation of hydrocarbons
- young males

#### Investigations

- renal biopsy: linear IgG deposits along basement membrane
- raised transfer factor secondary to pulmonary haemorrhages

#### Management

- plasma exchange
- steroids
- cyclophosphamide

**Question 17 of 93**

Next

A 72-year-old woman who has been on the ward for the past five days is noted by the nurses not to be passing much urine. She was admitted originally with pneumonia but has since developed diarrhoea. Blood tests show her creatinine has increased from 98 to 172  $\mu\text{mol/l}$ . Which one of the following tests is most useful when determining whether there is prerenal uraemia or acute tubular necrosis?

- ☐ A. Serum urea level
- ☐ B. Haemoglobin concentration
- ☐ C. Plasma osmolality
- ☐ D. Urinary urea
- ☐ E. Urinary sodium

Next question

**Acute renal failure: acute tubular necrosis vs. Prerenal uraemia**

Prerenal uraemia - kidneys hold on to sodium to preserve volume

	<b>Pre-renal uraemia</b>	<b>Acute tubular necrosis</b>
Urine sodium	< 20 mmol/L	> 30 mmol/L
Fractional sodium excretion*	< 1%	> 1%
Fractional urea excretion**	< 35%	> 35%
Urine:plasma osmolality	> 1.5	< 1.1
Urine:plasma urea	> 10:1	< 8:1
Specific gravity	> 1020	< 1010
Urine	'bland' sediment	brown granular casts
Response to fluid challenge	Yes	No

\*fractional sodium excretion =  $(\text{urine sodium}/\text{plasma sodium}) / (\text{urine creatinine}/\text{plasma creatinine}) \times 100$

\*\*fractional urea excretion =  $(\text{urine urea} / \text{blood urea}) / (\text{urine creatinine}/\text{plasma creatinine}) \times 100$

Which one of the following statements regarding the assessment of proteinuria in patients with chronic kidney disease is incorrect?

- ☐ A. Albumin:creatinine ratio (ACR) is more sensitive than protein:creatinine ratio (PCR)
- ☐ B. An ACR of 30 mg/mmol is approximately equal to a PCR of 50 mg/mmol
- ☐ C. An ACR sample is collected over 24 hours
- ☐ D. Women typically have higher ACR values
- ☐ E. An ACR of 3.1 mg/mmol in a diabetic man is clinically significant

Next question

### Chronic kidney disease: proteinuria

Proteinuria is an important marker of chronic kidney disease, especially for diabetic nephropathy. NICE recommend using the albumin:creatinine ratio (ACR) in preference to the protein:creatinine ratio (PCR) when identifying patients with proteinuria as it has greater sensitivity. For quantification and monitoring of proteinuria, PCR can be used as an alternative, although ACR is recommended in diabetics. Urine reagent strips are not recommended unless they express the result as an ACR

#### Approximate equivalent values

ACR (mg/mmol)	PCR (mg/mmol)	Urinary protein excretion (g/24 h)
30	50	0.5
70	100	1

#### Collecting an ACR sample

- by collecting a 'spot' sample it avoids the need to collect urine over a 24 hour period in order to detect or quantify proteinuria
- should be a first-pass morning urine specimen
- if the initial ACR is greater than 30 mg/mmol and less than 70 mg/mmol, confirm by a subsequent early morning sample. If the initial ACR is greater than 70 mg/mmol a repeat sample need not be tested

#### Interpreting the ACR results

- in non-diabetics an ACR greater than 30 mg/mmol is considered clinically significant proteinuria
- in diabetics microalbuminuria (ACR greater than 2.5 mg/mmol in men and ACR greater than 3.5 mg/mmol in women) is considered clinically significant

Which one of the following is least recognised as a cause of membranous glomerulonephritis?

<input type="radio"/>	A. Malaria
<input type="radio"/>	B. Lymphoma
<input type="radio"/>	C. Hepatitis B
<input type="radio"/>	D. Cryoglobulinaemia
<input type="radio"/>	E. Gold

Next question

### Membranous glomerulonephritis

Membranous glomerulonephritis is the commonest type of glomerulonephritis in adults and is the third most common cause of end-stage renal failure (ESRF). It usually presents with nephrotic syndrome or proteinuria.

Renal biopsy demonstrates:

- sub-epithelial immune complex (mainly IgG and C3) deposition in the glomerulus
- electron microscopy: the basement membrane is thickened with sub-epithelial electron dense deposits

Causes

- idiopathic
- infections: hepatitis B, malaria
- malignancy: lung cancer, lymphoma, leukaemia
- drugs: gold, penicillamine, NSAIDs
- systemic lupus erythematosus (class V disease)

Prognosis - rule of thirds

- one-third: spontaneous remission
- one-third: remain proteinuric
- one-third: develop ESRF

Management

- immunosuppression: corticosteroids alone have not been shown to be effective. A combination of corticosteroid + another agent such as chlorambucil is often used
- blood pressure control: ACE inhibitors have been shown to reduce proteinuria
- consider anticoagulation



**Question 20 of 93**[Next](#)

Autosomal dominant polycystic kidney disease type 1 is associated with a gene defect in:

- ☐ A. Chromosome 4
- ☐ B. Chromosome 8
- ☐ C. Chromosome 12
- ☒ D. Chromosome 16
- ☐ E. Chromosome 20

[Next question](#)

ADPKD type 1 = chromosome 16 = 85% of cases

**ADPKD**

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	ADPKD type 2
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

**Question 21 of 93**

Next

A 35-year-old female is admitted to hospital with hypovolaemic shock. CT abdomen reveals a haemorrhagic lesion in the right kidney. Following surgery and biopsy this is shown to be an angiomyolipomata. What is the most likely underlying diagnosis?

<input type="radio"/>	A. Neurofibromatosis
<input type="radio"/>	B. Budd-Chiari syndrome
<input type="radio"/>	C. Hereditary haemorrhagic telangiectasia
<input type="radio"/>	D. Von Hippel-Lindau syndrome
<input type="radio"/>	E. Tuberous sclerosis

Next question

**Tuberous sclerosis**

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous

## Cutaneous features

- depigmented 'ash-leaf' spots which fluoresce under UV light
- roughened patches of skin over lumbar spine (Shagreen patches)
- adenoma sebaceum: butterfly distribution over nose
- fibromata beneath nails (subungual fibromata)
- café-au-lait spots\* may be seen

## Neurological features

- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment

## Also

- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- gliomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata

\*these of course are more commonly associated with neurofibromatosis. However a 1998 study of 106 children with TS found café-au-lait spots in 28% of patients

Which one of the following causes of glomerulonephritis is associated with normal complement levels?

<input type="radio"/>	A. Post-streptococcal glomerulonephritis
<input type="radio"/>	B. Mesangiocapillary glomerulonephritis
<input type="radio"/>	C. Subacute bacterial endocarditis
<input type="radio"/>	D. Goodpasture's syndrome
<input type="radio"/>	E. Systemic lupus erythematosus

Next question

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen. Complement levels are normal

### Glomerulonephritis and low complement

Disorders associated with glomerulonephritis and low serum complement levels

- post-streptococcal glomerulonephritis
- subacute bacterial endocarditis
- systemic lupus erythematosus
- mesangiocapillary glomerulonephritis

**Question 23 of 93**

Next

An 18-year-old girl who is deaf and has a history of renal impairment is reviewed in clinic. She has previously been diagnosed with Alport's syndrome but is thinking about having children and asks about the risks of passing the condition on. What is the mode of inheritance of Alport's syndrome in the majority of cases?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. X-linked dominant   |
| <input type="radio"/> | B. Mitochondrial       |
| <input type="radio"/> | C. Autosomal recessive |
| <input type="radio"/> | D. Autosomal dominant  |
| <input type="radio"/> | E. X-linked recessive  |

Next question

Alport's syndrome - X-linked dominant (in the majority)

Around 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants also existing

**Alport's syndrome**

Alport's syndrome is usually inherited in an X-linked dominant pattern\*. It is due to a defect in the gene which codes for type IV collagen resulting in an abnormal glomerular-basement membrane (GBM). The disease is more severe in males with females rarely developing renal failure

A favourite question is an Alport's patient with a failing renal transplant. This may be caused by the presence of anti-GBM antibodies leading to a Goodpasture's syndrome like picture

Alport's syndrome usually presents in childhood. The following features may be seen:

- microscopic haematuria
- progressive renal failure
- bilateral sensorineural deafness
- lenticonus: protrusion of the lens surface into the anterior chamber
- retinitis pigmentosa

\*in around 85% of cases - 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants existing

**Question 24 of 93**

Next

A 73-year-old with a history of alcohol excess is admitted following a fall at home. On admission the following blood results are obtained:

Urea	3.5 mmol/l
Creatinine	110 $\mu$ mol/l
Creatine kinase	180 u/l

Three days later the blood results are as follows:

Urea	14.5 mmol/l
Creatinine	248 $\mu$ mol/l
Creatine kinase	4,400 u/l

Which one of the following would have been most likely to prevent the deterioration in renal function?

- ☐ A. Low dose dopamine
- ☐ B. Urinary acidification
- ☐ C. Intravenous fluids
- ☐ D. Frusemide
- ☐ E. Mannitol

Next question

Collapse + ARF --> rhabdomyolysis - treat with IV fluids

Intravenous fluids are the most important management step in the prevention of rhabdomyolysis in such patients

**Rhabdomyolysis**

Rhabdomyolysis will typically feature in the exam as a patient who has had a fall or prolonged epileptic seizure and is found to have acute renal failure on admission

**Features**

- acute renal failure with disproportionately raised creatinine
- elevated CK
- myoglobinuria
- hypocalcaemia (myoglobin binds calcium)
- elevated phosphate (released from myocytes)

## Causes

- seizure
- collapse/coma (e.g. elderly patients collapsed at home, found 8 hours later)
- ecstasy
- crush injury
- McArdle's syndrome
- drugs: statins

## Management

- IV fluids to maintain good urine output
- urinary alkalinization is sometimes used

A 10-year-old boy is taken to see the GP by his mother. For the past two days he has had a sore throat associated with blood in his urine. There is no significant past medical history. The GP suspects glomerulonephritis and refers the patient to hospital. What would a renal biopsy most likely show?

<input type="radio"/>	A. Proliferation of endothelial cells
<input type="radio"/>	B. No change
<input type="radio"/>	C. Mesangial hypercellularity
<input type="radio"/>	D. Basement membrane thickening
<input type="radio"/>	E. Capillary wall necrosis

[Next question](#)

This boy is likely to have IgA nephropathy. Histological features include mesangial hypercellularity and positive immunofluorescence for IgA & C3

### IgA nephropathy

#### Basics

- also called Berger's disease or mesangioproliferative glomerulonephritis
- commonest cause of glomerulonephritis worldwide
- pathogenesis unknown, ?mesangial deposition of IgA immune complexes
- histology: mesangial hypercellularity, positive immunofluorescence for IgA & C3

#### Differentiating between IgA nephropathy and post-streptococcal glomerulonephritis

- post-streptococcal glomerulonephritis is associated with low complement levels
- main symptom in post-streptococcal glomerulonephritis is proteinuria (although haematuria can occur)
- there is typically an interval between URTI and the onset of renal problems in post-streptococcal glomerulonephritis

#### Presentations

- young male, recurrent episodes of macroscopic haematuria
- typically associated with mucosal infections e.g., URTI
- nephrotic range proteinuria is rare
- renal failure

#### Associated conditions

- alcoholic cirrhosis

- coeliac disease/dermatitis herpetiformis

## Management

- steroids/immunosuppressants not be shown to be useful

## Prognosis

- 25% of patients develop ESRF
- markers of good prognosis: frank haematuria
- markers of poor prognosis: male gender, proteinuria (especially > 2 g/day), hypertension, smoking, hyperlipidaemia, ACE genotype DD



**Question 26 of 93**

Next

A 62-year-old man with chronic kidney disease secondary to diabetes mellitus is reviewed. When assessing his estimated glomerular filtration rate (eGFR), which one of the following variables is not required by the Modification of Diet in Renal Disease (MDRD) equation?

- ☐ A. Age
- ☐ B. Serum creatinine
- ☐ C. Ethnicity
- ☐ D. Gender
- ☐ E. Serum urea

Next question

eGFR variables - CAGE - Creatinine, Age, Gender, Ethnicity

**Chronic kidney disease: eGFR and classification**

Serum creatinine may not provide an accurate estimate of renal function due to differences in muscle. For this reason formulas were developed to help estimate the glomerular filtration rate (estimated GFR or eGFR). The most commonly used formula is the Modification of Diet in Renal Disease (MDRD) equation, which uses the following variables:

- serum creatinine
- age
- gender
- ethnicity

Factors which may affect the result

- pregnancy
- muscle mass (e.g. amputees, body-builders)
- eating red meat 12 hours prior to the sample being taken

CKD may be classified according to GFR:

CKD stage	GFR range
1	Greater than 90 ml/min, with some sign of kidney damage on other tests (if all the kidney tests* are normal, there is no CKD)
2	60-90 ml/min with some sign of kidney damage (if kidney tests* are normal, there is no CKD)

3a	45-59 ml/min, a moderate reduction in kidney function
3b	30-44 ml/min, a moderate reduction in kidney function
4	15-29 ml/min, a severe reduction in kidney function
5	Less than 15 ml/min, established kidney failure - dialysis or a kidney transplant may be needed

\*i.e. normal U&Es and no proteinuria

Which one of the following may be useful in the prevention of calcium renal stones?

<input type="radio"/>	A. Pyridoxine
<input type="radio"/>	B. Allopurinol
<input type="radio"/>	C. Lithium
<input type="radio"/>	D. Ferrous sulphate
<input type="radio"/>	E. Thiazide diuretics

Next question

The fact that thiazide diuretics cause hypercalcaemia is sometimes confused with their role in preventing calcium renal stones - the hypercalcaemia seen is secondary to increased distal tubular calcium resorption and hence lower calcium concentration in the urine

### Renal stones: management

#### Acute management of renal colic

Diclofenac 75 mg by intramuscular injection is the analgesia of choice for renal colic\*. A second dose can be given after 30 minutes if necessary

#### Prevention of renal stones

##### Calcium stones

- high fluid intake
- low animal protein, low salt diet (a low calcium diet has not been shown to be superior to a normocalcaemic diet)
- thiazide diuretics (increase distal tubular calcium resorption)
- stones < 5 mm will usually pass spontaneously
- lithotripsy, nephrolithotomy may be required

##### Oxalate stones

- cholestyramine reduces urinary oxalate secretion
- pyridoxine reduces urinary oxalate secretion

##### Uric acid stones

- allopurinol
- urinary alkalinization e.g. oral bicarbonate

\*PR diclofenac is an alternative

**Question 28 of 93**

Next

A 45-year-old man is seen in the Emergency Department with nausea, pallor and lethargy. He has no past medical history of note. A cannula is inserted and bloods show the following

Na <sup>+</sup>	140 mmol/l
K <sup>+</sup>	6.7 mmol/l
Bicarbonate	14 mmol/l
Urea	18.2 mmol/l
Creatinine	230 µmol/l

What is the most appropriate initial management?

- ☐ A. Nebulised salbutamol
- ☐ B. Intravenous bicarbonate
- ☐ C. Haemodialysis
- ☐ D. Insulin/dextrose infusion
- ☐ E. Intravenous calcium gluconate

Next question

The first priority in this patient is to stabilise the myocardium with intravenous calcium gluconate.

**Hyperkalaemia: management**

Untreated hyperkalaemia may cause life-threatening arrhythmias. Precipitating factors should be addressed (e.g. acute renal failure) and aggravating drugs stopped (e.g. ACE inhibitors). Management may be categorised by the aims of treatment

Stabilisation of the cardiac membrane

- intravenous calcium gluconate

Short-term shift in potassium from extracellular to intracellular fluid compartment

- combined insulin/dextrose infusion
- nebulised salbutamol

Removal of potassium from the body

- calcium resonium (orally or enema)
- loop diuretics
- dialysis

**Question 29 of 93**

Next

You review a 42-year-old woman six weeks following a renal transplant for focal segmental glomerulosclerosis. Following the procedure she was discharged on a combination of tacrolimus, mycophenolate, and prednisolone. She has now presented with a five day history of feeling generally unwell with anorexia, fatigue and arthralgia. On examination her sclera are jaundiced and she has widespread lymphadenopathy with hepatomegaly. What is the most likely diagnosis?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Hepatitis C        |
| <input type="radio"/> | B. Epstein-Barr virus |
| <input type="radio"/> | C. HIV                |
| <input type="radio"/> | D. Hepatitis B        |
| <input type="radio"/> | E. Cytomegalovirus    |

Next question

Cytomegalovirus is the most common and important viral infection in solid organ transplant recipients

Ganciclovir is the treatment of choice in such patients.

**Renal transplant: HLA typing and graft failure**

The human leucocyte antigen (HLA) system is the name given to the major histocompatibility complex (MHC) in humans. It is coded for on chromosome 6.

Some basic points on the HLA system

- class 1 antigens include A, B and C. Class 2 antigens include DP,DQ and DR
- when HLA matching for a renal transplant the relative importance of the HLA antigens are as follows DR > B > A

Graft survival

- 1 year = 90%, 10 years = 60% for cadaveric transplants
- 1 year = 95%, 10 years = 70% for living-donor transplants

Post-op problems

- ATN of graft
- vascular thrombosis
- urine leakage
- UTI

#### Hyperacute graft rejection (minutes to hours)

- due to pre-existent antibodies against donor HLA type 1 antigens (a type II hypersensitivity reaction)
- rarely seen due to HLA matching

#### Acute graft failure (< 6 months)

- usually due to mismatched HLA. Cell-mediated (cytotoxic T cells)
- other causes include cytomegalovirus infection
- may be reversible with steroids and immunosuppressants

#### Causes of chronic graft failure (> 6 months)

- both antibody and cell mediated mechanisms cause fibrosis to the transplanted kidney (chronic allograft nephropathy)
- recurrence of original renal disease (MCGN > IgA > FSGS)

A 43-year-old man has a work-up for hypertension. He has found to have blood + on a urine dipstick of a freshly voided sample. Which one of the following may account for this finding?

<input type="radio"/>	A. Smoking
<input type="radio"/>	B. Exercise
<input type="radio"/>	C. Obesity
<input type="radio"/>	D. Eating red meat the previous day
<input type="radio"/>	E. Use of ramipril

[Next question](#)

## Haematuria

The management of patients with haematuria is often difficult due to the absence of widely followed guidelines. It is sometimes unclear whether patients are best managed in primary care, by urologists or by nephrologists.

The terminology surrounding haematuria is changing. Microscopic or dipstick positive haematuria is increasingly termed non-visible haematuria whilst macroscopic haematuria is termed visible haematuria.

Causes of transient or spurious non-visible haematuria

- urinary tract infection
- menstruation
- vigorous exercise
- sexual intercourse

Causes of persistent non-visible haematuria

- cancer (bladder, renal, prostate)
- stones
- benign prostatic hyperplasia
- prostatitis
- urethritis e.g. *Chlamydia*
- renal causes: IgA nephropathy, thin basement membrane disease

## Management

Current evidence does not support screening for haematuria. The incidence of non-visible haematuria is similar in patients taking aspirin/warfarin to the general population hence these patients should also be investigated.

## Testing

- urine dipstick is the test of choice for detecting haematuria
- urine microscopy may be used but time to analysis significantly affects the number of red blood cells detected

## NICE urgent cancer referral guidelines

- of any age with painless macroscopic haematuria
- aged 40 years and older who present with recurrent or persistent urinary tract infection associated with haematuria
- aged 50 years and older who are found to have unexplained microscopic haematuria



Which one of the following types of glomerulonephritis is most characteristically associated with Goodpasture's syndrome?

<input type="radio"/>	A. Diffuse proliferative glomerulonephritis
<input type="radio"/>	B. Mesangiocapillary glomerulonephritis
<input type="radio"/>	C. Membranous glomerulonephritis
<input type="radio"/>	D. Rapidly progressive glomerulonephritis
<input type="radio"/>	E. Focal segmental glomerulosclerosis

Next question

Rapidly progressive glomerulonephritis, causes:

- Goodpasture's
- ANCA positive vasculitis

Goodpasture's syndrome is rare condition associated with both pulmonary haemorrhage and rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane (anti-GBM) antibodies against type IV collagen

### Glomerulonephritides

Knowing a few key facts is the best way to approach the difficult subject of glomerulonephritis:

#### Membranous glomerulonephritis

- presentation: proteinuria / nephrotic syndrome / chronic kidney disease
- cause: infections, rheumatoid drugs, malignancy
- 1/3 resolve, 1/3 respond to cytotoxics, 1/3 develop chronic kidney disease

IgA nephropathy - aka Berger's disease, mesangioproliferative GN

- typically young adult with haematuria following an URTI

#### Diffuse proliferative glomerulonephritis

- classical post-streptococcal glomerulonephritis in child
- presents as nephritic syndrome / acute kidney injury
- most common form of renal disease in SLE

### Minimal change disease

- typically a child with nephrotic syndrome (accounts for 80%)
- causes: Hodgkin's, NSAIDs
- good response to steroids

### Focal segmental glomerulosclerosis

- may be idiopathic or secondary to HIV, heroin
- presentation: proteinuria / nephrotic syndrome / chronic kidney disease

### Rapidly progressive glomerulonephritis - aka crescentic glomerulonephritis

- rapid onset, often presenting as acute kidney injury
- causes include Goodpasture's, ANCA positive vasculitis

### Mesangiocapillary glomerulonephritis (membranoproliferative)

- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

A patient with type 1 diabetes mellitus is reviewed in the nephrology outpatient clinic. He is known to have stage 1 diabetic nephropathy. Which of the following best describes his degree of renal involvement?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Latent phase            |
| <input type="radio"/> | B. Hyperfiltration         |
| <input type="radio"/> | C. End-stage renal failure |
| <input type="radio"/> | D. Overt nephropathy       |
| <input type="radio"/> | E. Microalbuminuria        |

[Next question](#)

For the purposes of the MRCP, increase in the glomerular filtration rate (GFR) is most characteristic of stage 1 diabetic nephropathy. It is however known that elevation of the GFR usually persists into stage 2

### Diabetic nephropathy: stages

Diabetic nephropathy may be classified as occurring in five stages\*:

#### Stage 1

- hyperfiltration: increase in GFR
- may be reversible

#### Stage 2 (silent or latent phase)

- most patients do not develop microalbuminuria for 10 years
- GFR remains elevated

#### Stage 3 (incipient nephropathy)

- microalbuminuria (albumin excretion of 30 - 300 mg/day, dipstick negative)

#### Stage 4 (overt nephropathy)

- persistent proteinuria (albumin excretion > 300 mg/day, dipstick positive)
- hypertension is present in most patients
- histology shows diffuse glomerulosclerosis and focal glomerulosclerosis (Kimmelstiel-Wilson nodules)

#### Stage 5

- end-stage renal disease, GFR typically  $< 10\text{ml/min}$
- renal replacement therapy needed

The timeline given here is for type 1 diabetics. Patients with type 2 diabetes mellitus (T2DM) progress through similar stages but in a different timescale - some T2DM patients may progress quickly to the later stages

**Question 33 of 93**

Next

A 13-year-old girl develops purpura on her lower limbs and buttocks associated with microscopic haematuria. A diagnosis of Henoch-Schonlein purpura is made. Her urea and electrolytes show mild renal impairment that is still present 4 weeks later, although she does not require any specific therapy. What is the most likely renal outcome?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Hypertension within 20 years |
| <input type="radio"/> | B. Persistent proteinuria       |
| <input type="radio"/> | C. End stage renal failure      |
| <input type="radio"/> | D. Full renal recovery          |
| <input type="radio"/> | E. Frequent relapses            |

Next question

**Henoch-Schonlein purpura**

Henoch-Schonlein purpura (HSP) is an IgA mediated small vessel vasculitis. There is a degree of overlap with IgA nephropathy (Berger's disease). HSP is usually seen in children following an infection

**Features**

- palpable purpuric rash (with localized oedema) over buttocks and extensor surfaces of arms and legs
- abdominal pain
- polyarthritits
- features of IgA nephropathy may occur e.g. haematuria, renal failure

**Treatment**

- analgesia for arthralgia
- treatment of nephropathy is generally supportive. There is inconsistent evidence for the use of steroids and immunosuppressants

**Prognosis**

- usually excellent, HSP is a self-limiting condition, especially in children without renal involvement
- around 1/3rd of patients have a relapse

**Question 34 of 93**[Next](#)

A 47-year-old woman presents with loin pain and haematuria. Urine dipstick demonstrates:

Blood	++++
Nitrites	POS
Leucocytes	+++
Protein	++

Urine culture shows a *Proteus* infection. An x-ray demonstrates a stag-horn calculus in the left renal pelvis. What is the most likely composition of the renal stone?

- ☐ A. Xanthine
- ☐ B. Calcium oxalate
- ☐ C. Struvite
- ☐ D. Cystine
- ☐ E. Urate

[Next question](#)**Stag-horn calculi**

- composed of **Struvite** (ammonium magnesium phosphate, triple phosphate)
- form in alkaline urine (ammonia producing bacteria such as *Ureaplasma urealyticum* and *Proteus* therefore predispose)

**Renal stones: imaging**

The table below summarises the appearance of different types of renal stone on x-ray

Type	Frequency	Radiograph appearance
Calcium oxalate	40%	Opaque
Mixed calcium oxalate/phosphate stones	25%	Opaque
Triple phosphate stones*	10%	Opaque
Calcium phosphate	10%	Opaque
Urate stones	5-10%	Radio-lucent
Cystine stones	1%	Semi-opaque, 'ground-glass' appearance
Xanthine stones	<1%	Radio-lucent

\*stag-horn calculi involve the renal pelvis and extend into at least 2 calyces. They develop in alkaline urine and are composed of struvite (ammonium magnesium phosphate, triple phosphate). *Ureaplasma urealyticum* and *Proteus* infections predispose to their formation

A 34-year-old man presents to the Emergency Department with abdominal pain. This started earlier on in the day and is getting progressively worse. The pain is located on his left flank and radiates down into his groin. He has had not had a similar pain before and is normally fit and well. Examination reveals a man who is flushed and sweaty but is otherwise unremarkable. What is the most suitable initial management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Oral ciprofloxacin  |
| <input type="radio"/> | B. IM diclofenac 75 mg   |
| <input type="radio"/> | C. Immediate abdominal ultrasound  |
| <input type="radio"/> | D. IM morphine 5 mg  |
| <input type="radio"/> | E. IM diclofenac 75 mg + start bendroflumethiazide to prevent further episodes |

This man may need to be referred acutely to the surgeons for pain relief and investigations to exclude obstruction. It would not be suitable to start bendroflumethiazide in the initial phase of the first episode. An immediate abdominal ultrasound is not necessary as neither his age nor symptoms point to a diagnosis of abdominal aneurysm.

### Renal stones: management

#### Acute management of renal colic

Diclofenac 75 mg by intramuscular injection is the analgesia of choice for renal colic\*. A second dose can be given after 30 minutes if necessary

#### Prevention of renal stones

Calcium stones

- high fluid intake
- low animal protein, low salt diet (a low calcium diet has not been shown to be superior to a normocalcaemic diet)
- thiazide diuretics (increase distal tubular calcium resorption)
- stones < 5 mm will usually pass spontaneously
- lithotripsy, nephrolithotomy may be required

Oxalate stones

- cholestyramine reduces urinary oxalate secretion
- pyridoxine reduces urinary oxalate secretion

Uric acid stones

- allopurinol
- urinary alkalization e.g. oral bicarbonate

\*PR diclofenac is an alternative



**Question 36 of 93**

Next

A 44-year-old man is referred to the renal team. He has a long history of chronic sinusitis and was investigated last year for haemoptysis but no cause was found. A number of recent urine dipstick tests has shown persistent microscopic haematuria.

Na <sup>+</sup>	140 mmol/l
K <sup>+</sup>	4.8 mmol/l
Urea	11.4 mmol/l
Creatinine	145 µmol/l

ESR	61 mm/hr
CRP	30 mg/l
anti-GBM	Negative
cANCA (PR3)	Positive
pANCA (MPO)	Negative
ANA	Negative

Given the likely diagnosis, what findings would be expected on renal biopsy?

<input type="radio"/>	A. Segmental tuft necrosis
<input type="radio"/>	B. Kimmelstiel-Wilson nodules
<input type="radio"/>	C. Crescentic glomerulonephritis
<input type="radio"/>	D. 'Full-house' immunoglobulin deposition
<input type="radio"/>	E. Membranous glomerulonephritis

Next question

**Wegener's granulomatosis**

Wegener's granulomatosis is an autoimmune condition associated with a necrotizing granulomatous vasculitis, affecting both the upper and lower respiratory tract as well as the kidneys

**Features**

- upper respiratory tract: epistaxis, sinusitis, nasal crusting
- lower respiratory tract: dyspnoea, haemoptysis
- glomerulonephritis ('pauci-immune', 80% of patients)
- saddle-shape nose deformity
- also: vasculitic rash, eye involvement (e.g. proptosis), cranial nerve lesions

## Investigations

- cANCA positive in > 90%, pANCA positive in 25%
- chest x-ray: wide variety of presentations, including cavitating lesions
- renal biopsy: crescentic glomerulonephritis

## Management

- steroids
- cyclophosphamide (90% response)
- plasma exchange
- median survival = 8-9 years

**Question 37 of 93**

Next

A 62-year-old man is reviewed in the renal clinic. He has been referred as his creatinine level increased from 90 to 173  $\mu\text{mol/l}$  after the introduction of ramipril. This had been started in an attempt to control his blood pressure. An ultrasound abdomen is reported as follows:

Both kidneys are small with the right measuring 5.8cm and the left 5.6cm

Normal liver, pancreas, spleen and bladder outline

What is the most appropriate next line investigation?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. Renal angiography                  |
| <input type="radio"/> | B. 24 hour urinary protein collection |
| <input type="radio"/> | C. Renal artery Doppler flow studies  |
| <input type="radio"/> | D. CT angiography                     |
| <input type="radio"/> | E. MR angiography                     |

Next question

**Renal vascular disease**

Renal vascular disease is most commonly due to atherosclerosis (> 95% of patients). It is associated with risk factors such as smoking and hypertension that cause atheroma elsewhere in the body. It may present as hypertension, chronic renal failure or 'flash' pulmonary oedema. In younger patients however fibromuscular dysplasia (FMD) needs to be considered. FMD is more common in young women and characteristically has a 'string of beads' appearance on angiography. Patients respond well to balloon angioplasty

**Investigation**

- MR angiography is now the investigation of choice
- CT angiography
- conventional renal angiography is less commonly performed used nowadays, but may still have a role when planning surgery

Each one of the following is associated with papillary necrosis, except:

<input type="radio"/>	A. Acute pyelonephritis
<input type="radio"/>	B. Tuberculosis
<input type="radio"/>	C. Chronic analgesia use
<input type="radio"/>	D. Syphilis
<input type="radio"/>	E. Sick cell disease

Next question

## Papillary necrosis

### Causes

- chronic analgesia use
- sickle cell disease
- TB
- acute pyelonephritis
- diabetes mellitus

### Features

- fever, loin pain, haematuria
- IVU - papillary necrosis with renal scarring - 'cup & spill'

Which one of the following types of glomerulonephritis is most characteristically associated with streptococcal infection in children?

<input type="radio"/>	A. Focal segmental glomerulosclerosis
<input type="radio"/>	B. Diffuse proliferative glomerulonephritis
<input type="radio"/>	C. Membranous glomerulonephritis
<input type="radio"/>	D. Mesangiocapillary glomerulonephritis
<input type="radio"/>	E. Rapidly progressive glomerulonephritis

Next question

Diffuse proliferative glomerulonephritis, causes:

- post-streptococcal
- SLE

## Glomerulonephritides

Knowing a few key facts is the best way to approach the difficult subject of glomerulonephritis:

Membranous glomerulonephritis

- presentation: proteinuria / nephrotic syndrome / chronic kidney disease
- cause: infections, rheumatoid drugs, malignancy
- 1/3 resolve, 1/3 respond to cytotoxics, 1/3 develop chronic kidney disease

IgA nephropathy - aka Berger's disease, mesangioproliferative GN

- typically young adult with haematuria following an URTI

Diffuse proliferative glomerulonephritis

- classical post-streptococcal glomerulonephritis in child
- presents as nephritic syndrome / acute kidney injury
- most common form of renal disease in SLE

Minimal change disease

- typically a child with nephrotic syndrome (accounts for 80%)
- causes: Hodgkin's, NSAIDs
- good response to steroids

#### Focal segmental glomerulosclerosis

- may be idiopathic or secondary to HIV, heroin
- presentation: proteinuria / nephrotic syndrome / chronic kidney disease

#### Rapidly progressive glomerulonephritis - aka crescentic glomerulonephritis

- rapid onset, often presenting as acute kidney injury
- causes include Goodpasture's, ANCA positive vasculitis

#### Mesangiocapillary glomerulonephritis (membranoproliferative)

- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

**Question 40 of 93**[Next](#)

A 70-year-old man has been admitted with abdominal pain. The surgeons wish to perform a contrast-enhanced CT but are concerned because he has chronic kidney disease stage 3. Other than ensuring adequate hydration, which one of the following can reduce the risk of contrast-induced nephropathy?

<input type="radio"/>	A. Oral sodium bicarbonate
<input type="radio"/>	B. Oral prednisolone
<input type="radio"/>	C. Oral N-acetylcysteine
<input type="radio"/>	D. Intravenous furosemide
<input type="radio"/>	E. Intravenous mannitol

[Next question](#)**Nephrotoxicity due to contrast media**

Contrast media nephrotoxicity may be defined as a 25% increase in creatinine occurring within 3 days of the intravascular administration of contrast media.

Risk factors include

- known renal impairment (especially diabetic nephropathy)
- age > 70 years
- dehydration
- cardiac failure
- the use of nephrotoxic drugs such as NSAIDs

Prevention

- ensure adequate hydration
- N-acetylcysteine (usually given orally) has been shown to reduce the incidence of contrast-nephropathy

**Question 41 of 93**

Next

A 54-year-old man who has end stage diabetic nephropathy is being assessed for a renal transplant. When assessing the HLA matching between donor and recipient what is the most important HLA antigen to match?

- |                       |       |
|-----------------------|-------|
| <input type="radio"/> | A. DP |
| <input type="radio"/> | B. B  |
| <input type="radio"/> | C. DR |
| <input type="radio"/> | D. C  |
| <input type="radio"/> | E. A  |

Next question

Renal transplant HLA matching - DR is the most important

**Renal transplant: HLA typing and graft failure**

The human leucocyte antigen (HLA) system is the name given to the major histocompatibility complex (MHC) in humans. It is coded for on chromosome 6.

Some basic points on the HLA system

- class 1 antigens include A, B and C. Class 2 antigens include DP,DQ and DR
- when HLA matching for a renal transplant the relative importance of the HLA antigens are as follows DR > B > A

Graft survival

- 1 year = 90%, 10 years = 60% for cadaveric transplants
- 1 year = 95%, 10 years = 70% for living-donor transplants

Post-op problems

- ATN of graft
- vascular thrombosis
- urine leakage
- UTI

Hyperacute graft rejection (minutes to hours)



- due to pre-existent antibodies against donor HLA type 1 antigens (a type II hypersensitivity reaction)
- rarely seen due to HLA matching

#### Acute graft failure (< 6 months)

- usually due to mismatched HLA. Cell-mediated (cytotoxic T cells)
- other causes include cytomegalovirus infection
- may be reversible with steroids and immunosuppressants

#### Causes of chronic graft failure (> 6 months)

- both antibody and cell mediated mechanisms cause fibrosis to the transplanted kidney (chronic allograft nephropathy)
- recurrence of original renal disease (MCGN > IgA > FSGS)

Which one of the following features is least likely to be seen in Henoch-Schonlein purpura?

<input type="radio"/>	A. Abdominal pain
<input type="radio"/>	B. Renal failure
<input type="radio"/>	C. Polyarthrititis
<input type="radio"/>	D. Thrombocytopenia
<input type="radio"/>	E. Purpuric rash over buttocks

Next question

### Henoch-Schonlein purpura

Henoch-Schonlein purpura (HSP) is an IgA mediated small vessel vasculitis. There is a degree of overlap with IgA nephropathy (Berger's disease). HSP is usually seen in children following an infection

#### Features

- palpable purpuric rash (with localized oedema) over buttocks and extensor surfaces of arms and legs
- abdominal pain
- polyarthrititis
- features of IgA nephropathy may occur e.g. haematuria, renal failure

#### Treatment

- analgesia for arthralgia
- treatment of nephropathy is generally supportive. There is inconsistent evidence for the use of steroids and immunosuppressants

#### Prognosis

- usually excellent, HSP is a self-limiting condition, especially in children without renal involvement
- around 1/3rd of patients have a relapse

Which one of the following is least associated with retroperitoneal fibrosis?

<input type="radio"/>	A. Riedel's thyroiditis
<input type="radio"/>	B. Previous radiotherapy
<input type="radio"/>	C. Inflammatory abdominal aortic aneurysm
<input type="radio"/>	D. Methysergide
<input type="radio"/>	E. Sulphonamides

Next question

### Retroperitoneal fibrosis

Lower back pain is the most common presenting feature

Associations

- Riedel's thyroiditis
- previous radiotherapy
- sarcoidosis
- inflammatory abdominal aortic aneurysm
- drugs: methysergide

**Question 44 of 93**

Next

A 40-year-old woman with rheumatoid arthritis is diagnosed as having type 1 renal tubular acidosis. Which one of the following features is most likely to be seen as a consequence?

<input type="radio"/>	A. Hyperkalaemia
<input type="radio"/>	B. Osteomalacia
<input type="radio"/>	C. Decreased bicarbonate reabsorption in the proximal tubule
<input type="radio"/>	D. Raised anion gap metabolic acidosis
<input type="radio"/>	E. Nephrocalcinosis

Next question

Osteomalacia is more commonly seen in type 2 renal tubular acidosis.

**Renal tubular acidosis**

All three types of renal tubular acidosis (RTA) are associated with hyperchloraemic metabolic acidosis (normal anion gap)

**Type 1 RTA (distal)**

- inability to generate acid urine (secrete H<sup>+</sup>) in distal tubule
- causes hypokalaemia
- complications include nephrocalcinosis and renal stones
- causes include idiopathic, RA, SLE, Sjogren's

**Type 2 RTA (proximal)**

- decreased HCO<sub>3</sub><sup>-</sup> reabsorption in proximal tubule
- causes hypokalaemia
- complications include osteomalacia
- causes include idiopathic, as part of Fanconi syndrome, Wilson's disease, cystinosis, outdated tetracyclines

**Type 4 RTA (hyperkalaemic)**

- causes hyperkalaemia
- causes include hypoaldosteronism, diabetes

**Question 45 of 93**

Next

A 45-year-old woman with nephrotic syndrome is noted to have marked loss of subcutaneous tissue from the face. What is the most likely underlying cause of her renal disease?

<input type="radio"/>	A. Mesangiocapillary glomerulonephritis type II
<input type="radio"/>	B. Focal segmental glomerulosclerosis
<input type="radio"/>	C. Minimal change glomerulonephritis
<input type="radio"/>	D. Renal vein thrombosis
<input type="radio"/>	E. Membranous glomerulonephritis

Next question

**Mesangiocapillary glomerulonephritis (membranoproliferative)**

- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

This patient has partial lipodystrophy which is associated with mesangiocapillary glomerulonephritis type II

**Mesangiocapillary glomerulonephritis****Overview**

- also known as membranoproliferative glomerulonephritis
- may present as nephrotic syndrome, haematuria or proteinuria
- poor prognosis

**Type 1**

- subendothelial immune deposits
- cause: cryoglobulinaemia, hepatitis C

**Type 2 - 'dense deposit disease'**

- intramembranous deposits of electron dense material
- causes: partial lipodystrophy, factor H deficiency
- reduced serum complement
- C3b nephritic factor (an antibody against C3bBb) found in 70%

**Type 3**

- causes: hepatitis B and C

## Management

- steroids may be effective

**Question 46 of 93**

Next

A 65-year-old man with a history of hypertension is reviewed. As part of routine blood tests to monitor his renal function whilst taking ramipril the following blood tests are received:

Na <sup>+</sup>	140 mmol/l
K <sup>+</sup>	4.8 mmol/l
Urea	6.2 mmol/l
Creatinine	102 µmol/l
eGFR	68 ml/min

A urine dipstick is subsequently performed which is normal and a renal ultrasound shows normal sized kidneys with no abnormality detected. What stage of chronic kidney disease does this patient have?

- ☐ A. No chronic kidney disease
- ☐ B. Chronic kidney disease stage 4
- ☐ C. Chronic kidney disease stage 3
- ☐ D. Chronic kidney disease stage 2
- ☐ E. Chronic kidney disease stage 1

Next question

CKD: only diagnose stages 1 & 2 if supporting evidence to accompany eGFR

Chronic kidney disease is only diagnosed in this situation if supporting tests such as urinalysis or renal ultrasound are abnormal

**Chronic kidney disease: eGFR and classification**

Serum creatinine may not provide an accurate estimate of renal function due to differences in muscle. For this reason formulas were developed to help estimate the glomerular filtration rate (estimated GFR or eGFR). The most commonly used formula is the Modification of Diet in Renal Disease (MDRD) equation, which uses the following variables:

- serum creatinine
- age
- gender
- ethnicity

Factors which may affect the result

- pregnancy

- muscle mass (e.g. amputees, body-builders)
- eating red meat 12 hours prior to the sample being taken

CKD may be classified according to GFR:

CKD stage	GFR range
1	Greater than 90 ml/min, with some sign of kidney damage on other tests (if all the kidney tests* are normal, there is no CKD)
2	60-90 ml/min with some sign of kidney damage (if kidney tests* are normal, there is no CKD)
3a	45-59 ml/min, a moderate reduction in kidney function
3b	30-44 ml/min, a moderate reduction in kidney function
4	15-29 ml/min, a severe reduction in kidney function
5	Less than 15 ml/min, established kidney failure - dialysis or a kidney transplant may be needed

\*i.e. normal U&Es and no proteinuria



### Question 47 of 93

Next

Which of the following factors would suggest that a patient has established acute tubular necrosis rather than pre-renal uraemia?

- ☐ A. Urine sodium = 10 mmol/L
- ☐ B. Fractional urea excretion = 20%
- ☐ C. Increase in urine output following fluid challenge
- ☐ D. Specific gravity = 1025
- ☐ E. Fractional sodium excretion = 1.5%

Next question

ATN or prerenal uraemia? In prerenal uraemia think of the kidneys holding on to sodium to preserve volume

### Acute renal failure: acute tubular necrosis vs. Prerenal uraemia

Prerenal uraemia - kidneys hold on to sodium to preserve volume

	Pre-renal uraemia	Acute tubular necrosis
Urine sodium	< 20 mmol/L	> 30 mmol/L
Fractional sodium excretion*	< 1%	> 1%
Fractional urea excretion**	< 35%	> 35%
Urine:plasma osmolality	> 1.5	< 1.1
Urine:plasma urea	> 10:1	< 8:1
Specific gravity	> 1020	< 1010
Urine	'bland' sediment	brown granular casts
Response to fluid challenge	Yes	No

\*fractional sodium excretion = (urine sodium/plasma sodium) / (urine creatinine/plasma creatinine) x 100

\*\*fractional urea excretion = (urine urea /blood urea ) / (urine creatinine/plasma creatinine) x 100

**Question 48 of 93**

Next

A 20-year-old man presents with facial and ankle swelling. This has slowly been developing over the past week. During the review of systems he describes passing 'frothy' urine. A urine dipstick shows protein +++. What is the most likely cause of this presentation?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Minimal change disease                   |
| <input type="radio"/> | B. IgA nephropathy                          |
| <input type="radio"/> | C. Membranoproliferative glomerulonephritis |
| <input type="radio"/> | D. Polycystic kidney disease                |
| <input type="radio"/> | E. Membranous glomerulonephritis            |

Next question

Nephrotic syndrome in children / young adults - minimal change glomerulonephritis

Minimal change glomerulonephritis nearly always presents as nephrotic syndrome, accounting for 75% of cases in children and 25% in adults. The majority of cases are idiopathic and respond well to steroids.

Membranous glomerulonephritis would be unusual in a 20-year-old.

**Minimal change glomerulonephritis**

Minimal change glomerulonephritis nearly always presents as nephrotic syndrome, accounting for 75% of cases in children and 25% in adults

The majority of cases are idiopathic, but in around 10-20% a cause is found:

- drugs: NSAIDs, rifampicin
- Hodgkin's lymphoma, thymoma
- infectious mononucleosis

**Features**

- nephrotic syndrome
- normotension - hypertension is rare
- highly selective proteinuria\*
- renal biopsy: electron microscopy shows fusion of podocytes

**Management**

- majority of cases (80%) are steroid responsive

- cyclophosphamide is the next step for steroid resistant cases

Prognosis is overall good, although relapse is common. Roughly:

- 1/3 have just one episode
- 1/3 have infrequent relapses
- 1/3 have frequent relapses which stop before adulthood

\*only intermediate-sized proteins such as albumin and transferrin leak through the glomerulus

Which one of the following is least associated with focal segmental glomerulosclerosis?

<input type="radio"/>	A. Alport's syndrome
<input type="radio"/>	B. Heroin
<input type="radio"/>	C. Sickie-cell anaemia
<input type="radio"/>	D. Bleomycin
<input type="radio"/>	E. HIV infection

Next question

### Focal segmental glomerulosclerosis

Focal segmental glomerulosclerosis is cause of nephrotic syndrome and chronic kidney disease. It generally presents in young adults.

#### Causes

- idiopathic
- secondary to other renal pathology e.g. IgA nephropathy, reflux nephropathy
- HIV
- heroin
- Alport's syndrome
- sickle-cell

Focal segmental glomerulosclerosis is noted for having a high recurrence rate in renal transplants

Fanconi syndrome is associated with each one of the following, except:

<input type="radio"/>	A. Hydronephrosis
<input type="radio"/>	B. Osteomalacia
<input type="radio"/>	C. Aminoaciduria
<input type="radio"/>	D. Glycosuria
<input type="radio"/>	E. Proximal renal tubular acidosis

Next question

### Fanconi syndrome

Fanconi syndrome describes a generalised disorder of renal tubular transport resulting in:

- type 2 (proximal) renal tubular acidosis
- aminoaciduria
- glycosuria
- phosphaturia
- osteomalacia

### Causes

- cystinosis (most common cause in children)
- Sjogren's syndrome
- multiple myeloma
- nephrotic syndrome
- Wilson's disease

Which one of the following is least recognised as an indication for plasma exchange?

<input type="radio"/>	A. Guillain-Barre syndrome
<input type="radio"/>	B. Churg-Strauss syndrome
<input type="radio"/>	C. Myasthenia gravis
<input type="radio"/>	D. Cerebral malaria
<input type="radio"/>	E. Goodpasture's syndrome

Next question

Cerebral malaria is not a standard indication for plasma exchange. Exchange transfusions have been tried but it is generally only justified when peripheral parasitemia is greater than 10% of circulating erythrocytes. The role of blood transfusions remains controversial, as they are both expensive and potentially dangerous in many malaria areas

### Plasma exchange

Indications for plasma exchange

- Guillain-Barre syndrome
- myasthenia gravis
- Goodpasture's syndrome
- ANCA positive vasculitis e.g. Wegener's, Churg-Strauss
- TTP/HUS
- cryoglobulinaemia
- hyperviscosity syndrome e.g. secondary to myeloma

**Question 52 of 93**[Next](#)

A 26-year-old man with loin pain and haematuria is found to have autosomal dominant polycystic kidney disease. A defect in which one of the following genes is likely to be responsible?

- ☐ A. Fibrillin-2 gene
- ☐ B. Polycystin gene
- ☐ C. Fibrillin-1 gene
- ☐ D. Von Hippel-Lindau gene
- ☐ E. PKD1 gene

[Next question](#)

Most cases of autosomal dominant polycystic kidney disease (ADPKD) are due to a mutation in the PKD1 gene. The PKD1 gene encodes for a polycystin-1, a large cell-surface glycoprotein of unknown function

**ADPKD**

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	ADPKD type 2
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

A 62-year-old man is diagnosed with renal cell cancer. Which one of the following hormones is least likely to be present in excessive levels?

<input type="radio"/>	A. Erythropoietin
<input type="radio"/>	B. Parathyroid hormone
<input type="radio"/>	C. Growth hormone
<input type="radio"/>	D. ACTH
<input type="radio"/>	E. Renin

[Next question](#)

## Renal cell cancer

Renal cell cancer is also known as hypernephroma and accounts for 85% of primary renal neoplasms. It arises from proximal renal tubular epithelium

### Associations\*

- more common in middle-aged men
- smoking
- von Hippel-Lindau syndrome
- tuberous sclerosis

### Features

- classical triad: haematuria, loin pain, abdominal mass
- pyrexia of unknown origin
- left varicocele (due to occlusion of left testicular vein)
- endocrine effects: may secrete erythropoietin (polycythaemia), parathyroid hormone (hypercalcaemia), renin, ACTH
- 25% have metastases at presentation

### Management

- radical nephrectomy for confined disease
- alpha-interferon and interleukin-2 have been used to reduce tumour size and also treat patients with metastases
- receptor tyrosine kinase inhibitors (e.g. sorafenib, sunitinib) have been shown to have superior efficacy compared to interferon-alpha

\*incidence of renal cell cancer is only slightly increased in patients with autosomal dominant polycystic kidney disease



**Question 54 of 93**

Next

A 5-year-old boy is seen in the Emergency Department due to lethargy and pallor. There is no recent history of diarrhoea. The following results are obtained:

Hb	8.4 g/dl
Platelets	$30 \times 10^9/l$
Urea	24 mmol/l
Creatinine	164 $\mu$ mol/l

Urinalysis reveals proteinuria and haematuria. What is the most appropriate management?

- ☐ A. IV cyclophosphamide
- ☐ B. Ciprofloxacin
- ☐ C. Oral prednisolone
- ☐ D. IV methylprednisolone followed by oral prednisolone
- ☐ E. Plasma exchange

Next question

There is no role for antibiotics, steroids or immunosuppressants in haemolytic uraemic syndrome (HUS). Plasma exchange may be indicated, particularly in severe cases of HUS not associated with diarrhoea

**Haemolytic uraemic syndrome**

Haemolytic uraemic syndrome is generally seen in young children and produces a triad of:

- acute renal failure
- microangiopathic haemolytic anaemia
- thrombocytopenia

**Causes**

- post-dysentery - classically E coli O157:H7 ('verotoxigenic', 'enterohaemorrhagic')
- tumours
- pregnancy
- ciclosporin, the Pill
- systemic lupus erythematosus
- HIV

**Investigations**

- full blood count: anaemia, thrombocytopaenia, fragmented blood film

- U&E: acute renal failure
- stool culture

## Management

- treatment is supportive e.g. Fluids, blood transfusion and dialysis if required
- there is no role for antibiotics, despite the preceding diarrhoeal illness in many patients
- the indications for plasma exchange in HUS are complicated. As a general rule plasma exchange is reserved for severe cases of HUS not associated with diarrhoea

A 33-year-old man with a history of coeliac disease is admitted for investigation of recurrent macroscopic haematuria. His urine is typically brown and there is no history of passing clots. What is the most likely diagnosis?

<input type="radio"/>	A. Diffuse proliferative glomerulonephritis
<input type="radio"/>	B. IgA nephropathy
<input type="radio"/>	C. Membranous glomerulonephritis
<input type="radio"/>	D. Minimal change disease
<input type="radio"/>	E. Rapidly progressive glomerulonephritis

[Next question](#)

This man has IgA nephropathy which is associated with coeliac disease

### IgA nephropathy

#### Basics

- also called Berger's disease or mesangioproliferative glomerulonephritis
- commonest cause of glomerulonephritis worldwide
- pathogenesis unknown, ?mesangial deposition of IgA immune complexes
- histology: mesangial hypercellularity, positive immunofluorescence for IgA & C3

#### Differentiating between IgA nephropathy and post-streptococcal glomerulonephritis

- post-streptococcal glomerulonephritis is associated with low complement levels
- main symptom in post-streptococcal glomerulonephritis is proteinuria (although haematuria can occur)
- there is typically an interval between URTI and the onset of renal problems in post-streptococcal glomerulonephritis

#### Presentations

- young male, recurrent episodes of macroscopic haematuria
- typically associated with mucosal infections e.g., URTI
- nephrotic range proteinuria is rare
- renal failure

#### Associated conditions

- alcoholic cirrhosis
- coeliac disease/dermatitis herpetiformis

## Management

- steroids/immunosuppressants not be shown to be useful

## Prognosis

- 25% of patients develop ESRF
- markers of good prognosis: frank haematuria
- markers of poor prognosis: male gender, proteinuria (especially > 2 g/day), hypertension, smoking, hyperlipidaemia, ACE genotype DD

**Question 56 of 93**

Next

You are reviewing a 65-year-old in the renal clinic. He has been on haemodialysis for chronic kidney disease for the past 6 years. What is he most likely to die from?

<input type="radio"/>	A. Hyperkalaemia
<input type="radio"/>	B. Malignancy
<input type="radio"/>	C. Dilated cardiomyopathy
<input type="radio"/>	D. Dialysis related sepsis
<input type="radio"/>	E. Ischaemic heart disease

Next question

CKD on haemodialysis - most likely cause of death is IHD

Cardiovascular events account for 50% of the mortality in patients receiving dialysis.

**Chronic kidney disease: causes**

Common causes of chronic kidney disease

- diabetic nephropathy
- chronic glomerulonephritis
- chronic pyelonephritis
- hypertension
- adult polycystic kidney disease

Which one of the following is not a feature of HIV-associated nephropathy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Small kidneys                                      |
| <input type="radio"/> | B. Normotension                                       |
| <input type="radio"/> | C. Elevated urea and creatinine                       |
| <input type="radio"/> | D. Proteinuria  |
| <input type="radio"/> | E. Focal segmental glomerulosclerosis on renal biopsy |

Next question

### HIV: renal involvement

Renal involvement in HIV patients may occur as a consequence of treatment or the virus itself. Protease inhibitors such as indinavir can precipitate intratubular crystal obstruction

HIV-associated nephropathy (HIVAN) accounts for up to 10% of end-stage renal failure cases in the United States. Antiretroviral therapy has been shown to alter the course of the disease. There are five key features of HIVAN:

- massive proteinuria
- normal or large kidneys
- focal segmental glomerulosclerosis with focal or global capillary collapse on renal biopsy
- elevated urea and creatinine
- normotension

A 62-year-old man attends your clinic. He has a history of hypertension and atrial fibrillation for which he is anticoagulated with warfarin. A urine dipstick taken 8 weeks ago during a routine hypertension clinic appointment showed blood +. This has been repeated on two further occasions. What is the most appropriate action?

<input type="radio"/>	A. Take no further action
<input type="radio"/>	B. Send a 24-urine sample for protein estimation
<input type="radio"/>	C. Renal biopsy
<input type="radio"/>	D. Cystoscopy
<input type="radio"/>	E. Confirm with urine microscopy

[Next question](#)

The incidence of non-visible haematuria is similar in patients taking warfarin to the general population therefore these patients should be investigated as normal.

### Haematuria

The management of patients with haematuria is often difficult due to the absence of widely followed guidelines. It is sometimes unclear whether patients are best managed in primary care, by urologists or by nephrologists.

The terminology surrounding haematuria is changing. Microscopic or dipstick positive haematuria is increasingly termed non-visible haematuria whilst macroscopic haematuria is termed visible haematuria.

Causes of transient or spurious non-visible haematuria

- urinary tract infection
- menstruation
- vigorous exercise
- sexual intercourse

Causes of persistent non-visible haematuria

- cancer (bladder, renal, prostate)
- stones
- benign prostatic hyperplasia
- prostatitis
- urethritis e.g. *Chlamydia*
- renal causes: IgA nephropathy, thin basement membrane disease

### Management

Current evidence does not support screening for haematuria. The incidence of non-visible haematuria is similar

in patients taking aspirin/warfarin to the general population hence these patients should also be investigated.

## Testing

- urine dipstick is the test of choice for detecting haematuria
- urine microscopy may be used but time to analysis significantly affects the number of red blood cells detected

## NICE urgent cancer referral guidelines

- of any age with painless macroscopic haematuria
- aged 40 years and older who present with recurrent or persistent urinary tract infection associated with haematuria
- aged 50 years and older who are found to have unexplained microscopic haematuria



A 61-year-old man with a history of hypertension presents with central chest pain. Acute coronary syndrome is diagnosed and conventional management is given. A few days later a diagnostic coronary angiogram is performed. The following week a deteriorating of renal function is noted associated with a purpuric rash on his feet. What is the most likely diagnosis?

<input type="radio"/>	A. Aspirin-induced interstitial nephritis
<input type="radio"/>	B. Heparin-induced thrombocytopenia
<input type="radio"/>	C. Renal artery stenosis
<input checked="" type="radio"/>	D. Cholesterol embolisation
<input type="radio"/>	E. Antiphospholipid syndrome

[Next question](#)

Cholesterol embolisation is a well-documented complication of coronary angiography

### Cholesterol embolisation

#### Overview

- cholesterol emboli may break off causing renal disease
- seen more commonly in arteriopathies, abdominal aortic aneurysms

#### Features

- eosinophilia
- purpura
- renal failure
- livedo reticularis

A 62-year-old man with a diabetic nephropathy and hypertension is reviewed. His current medication is insulin, bendroflumethiazide, ramipril and amlodipine. On examination blood pressure is 144/78 mmHg. Blood tests reveal the following:

Na <sup>+</sup>	139 mmol/l
K <sup>+</sup>	4.9 mmol/l
Urea	12.8 mmol/l
Creatinine	215 µmol/l
eGFR	29 ml/min

Renal function was similar to 3 months ago. What is the most appropriate action?

- ☐ A. No change to his medication
- ☐ B. Switch bendroflumethiazide to furosemide
- ☐ C. Add a beta-blocker
- ☐ D. Add spironolactone
- ☐ E. Stop ramipril

Next question

As the eGFR is 29 ml/min switching bendroflumethiazide to furosemide would be the next step in controlling his blood pressure. Please see the guidelines in the external links section

### Chronic kidney disease: hypertension

The majority of patients with chronic kidney disease (CKD) will require more than two drugs to treat hypertension. ACE inhibitors are first line and are particularly helpful in proteinuric renal disease (e.g. diabetic nephropathy). As these drugs tend to reduce filtration pressure a small fall in glomerular filtration pressure (GFR) and rise in creatinine can be expected. NICE suggest that a decrease in eGFR of up to 25% or a rise in creatinine of up to 30% is acceptable, although any rise should prompt careful monitoring and exclusion of other causes (e.g. NSAIDs). A rise greater than this may indicate underlying renovascular disease.

Furosemide is useful as anti-hypertensive in patients with CKD, particularly when the GFR falls to below 45 ml/min\*. It has the added benefit of lowering serum potassium. High doses are usually required. If the patient becomes at risk of dehydration (e.g. Gastroenteritis) then consideration should be given to temporarily stopping the drug

\*the NKF K/DOQI guidelines suggest a lower cut-off of less than 30 ml/min

You review a 65-year-old man with stage 5 chronic kidney disease in the renal outpatient clinic. He has recently been started on erythropoietin injections. Which one of the following is the main benefit of this treatment?

<input type="radio"/>	A. Reduced proteinuria
<input type="radio"/>	B. Improved exercise tolerance
<input type="radio"/>	C. Reduced blood pressure
<input type="radio"/>	D. Improved renal function
<input type="radio"/>	E. Reduced long-term all-cause mortality

Next question

Erythropoietin treats CKD associated anaemia which in turn would improve exercise tolerance. It does not improve renal function.

### Erythropoietin

Erythropoietin is a haematopoietic growth factor that stimulates the production of erythrocytes. The main uses of erythropoietin are to treat the anaemia associated with chronic kidney disease and that associated with cytotoxic therapy.

Side-effects of erythropoietin

- accelerated hypertension potentially leading to encephalopathy and seizures (blood pressure increases in 25% of patients)
- bone aches
- flu-like symptoms
- skin rashes, urticaria
- pure red cell aplasia\* (due to antibodies against erythropoietin)
- raised PCV increases risk of thrombosis (e.g. Fistula)
- iron deficiency 2nd to increased erythropoiesis

There are a number of reasons why patients may fail to respond to erythropoietin therapy:

- iron deficiency
- inadequate dose
- concurrent infection/inflammation
- hyperparathyroid bone disease
- aluminium toxicity

\*the risk is greatly reduced with darbepoetin

**Question 62 of 93**

Next

A 71-year-old man with chronic kidney disease stage 3 is reviewed in the cardiology clinic. He is known to have hypertension and ischaemic heart disease but a recent fasting glucose result confirmed he is not diabetic. A recent early morning urine result is reported as follows:

Albumin:creatinine ratio	5.2 mg/mmol
--------------------------	-------------

What is the most appropriate action?

- ☐ A. Refer to a nephrologist
- ☐ B. No action as not clinically significant
- ☐ C. Obtain a 24-hour urine collection
- ☐ D. Repeat using a late-evening sample
- ☐ E. Arrange renovascular imaging

As he is not diabetic this result is not clinically significant

**Chronic kidney disease: proteinuria**

Proteinuria is an important marker of chronic kidney disease, especially for diabetic nephropathy. NICE recommend using the albumin:creatinine ratio (ACR) in preference to the protein:creatinine ratio (PCR) when identifying patients with proteinuria as it has greater sensitivity. For quantification and monitoring of proteinuria, PCR can be used as an alternative, although ACR is recommended in diabetics. Urine reagent strips are not recommended unless they express the result as an ACR

**Approximate equivalent values**

ACR (mg/mmol)	PCR (mg/mmol)	Urinary protein excretion (g/24 h)
30	50	0.5
70	100	1

**Collecting an ACR sample**

- by collecting a 'spot' sample it avoids the need to collect urine over a 24 hour period in order to detect or quantify proteinuria
- should be a first-pass morning urine specimen
- if the initial ACR is greater than 30 mg/mmol and less than 70 mg/mmol, confirm by a subsequent early morning sample. If the initial ACR is greater than 70 mg/mmol a repeat sample need not be tested

**Interpreting the ACR results**

- in non-diabetics an ACR greater than 30 mg/mmol is considered clinically significant proteinuria
- in diabetics microalbuminuria (ACR greater than 2.5 mg/mmol in men and ACR greater than 3.5 mg/mmol in women) is considered clinically significant

Which one of the following types of glomerulonephritis is most characteristically associated with Wegener's granulomatosis?

<input type="radio"/>	A. Mesangiocapillary glomerulonephritis
<input type="radio"/>	B. Membranous glomerulonephritis
<input checked="" type="radio"/>	C. Rapidly progressive glomerulonephritis
<input type="radio"/>	D. Focal segmental glomerulosclerosis
<input type="radio"/>	E. Diffuse proliferative glomerulonephritis

[Next question](#)

Rapidly progressive glomerulonephritis, causes:

- Goodpasture's
- ANCA positive vasculitis

## Glomerulonephritides

Knowing a few key facts is the best way to approach the difficult subject of glomerulonephritis:

Membranous glomerulonephritis

- presentation: proteinuria / nephrotic syndrome / chronic kidney disease
- cause: infections, rheumatoid drugs, malignancy
- 1/3 resolve, 1/3 respond to cytotoxics, 1/3 develop chronic kidney disease

IgA nephropathy - aka Berger's disease, mesangioproliferative GN

- typically young adult with haematuria following an URTI

Diffuse proliferative glomerulonephritis

- classical post-streptococcal glomerulonephritis in child
- presents as nephritic syndrome / acute kidney injury
- most common form of renal disease in SLE

Minimal change disease

- typically a child with nephrotic syndrome (accounts for 80%)
- causes: Hodgkin's, NSAIDs
- good response to steroids

#### Focal segmental glomerulosclerosis

- may be idiopathic or secondary to HIV, heroin
- presentation: proteinuria / nephrotic syndrome / chronic kidney disease

#### Rapidly progressive glomerulonephritis - aka crescentic glomerulonephritis

- rapid onset, often presenting as acute kidney injury
- causes include Goodpasture's, ANCA positive vasculitis

#### Mesangiocapillary glomerulonephritis (membranoproliferative)

- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

**Question 64 of 93**

Next

A 39-year-old woman with systemic lupus erythematosus presents for review in the rheumatology clinic. Dipstick urine on arrival at clinic shows protein ++. Further investigations reveal the following

Bicarbonate	22 mmol/l
Urea	7.1 mmol/l
Creatinine	134 µmol/l
24-hour urinary protein	2.6 g

What is the renal biopsy most likely to show?

- ☐ A. Diffuse proliferative glomerulonephritis
- ☐ B. Mesangiocapillary glomerulonephritis
- ☐ C. Rapidly progressive glomerulonephritis
- ☐ D. Membranous glomerulonephritis
- ☐ E. Minimal change disease

Next question

Diffuse proliferative glomerulonephritis is the most common and severe form of renal disease in SLE patients

Diffuse proliferative glomerulonephritis is the most common and severe form of renal disease in SLE patients

**SLE: renal complications**

WHO classification

- class I: normal kidney
- class II: mesangial glomerulonephritis
- class III: focal (and segmental) proliferative glomerulonephritis
- class IV: diffuse proliferative glomerulonephritis
- class V: diffuse membranous glomerulonephritis
- class VI: sclerosing glomerulonephritis

Class IV (diffuse proliferative glomerulonephritis) is the most common and severe form

Management

- treat hypertension
- corticosteroids if clinical evidence of disease
- immunosuppressants e.g. azathiopine/cyclophosphamide

**Question 65 of 93**

Next

A two-year old boy presents with an abdominal mass. Which of the following is associated with Wilm's tumour (nephroblastoma)?

<input type="radio"/>	A. Deletion on short arm of chromosome 12
<input type="radio"/>	B. Tuberose sclerosis
<input type="radio"/>	C. Beckwith-Wiedemann syndrome
<input type="radio"/>	D. Autosomal dominant polycystic kidney disease
<input type="radio"/>	E. Autosomal recessive polycystic kidney disease

Next question

Beckwith-Wiedemann syndrome is a inherited condition associated with organomegaly, macroglossia, abdominal wall defects, Wilm's tumour and neonatal hypoglycaemia.

**Wilms' tumour**

Wilms' nephroblastoma is one of the most common childhood malignancies. It typically presents in children under 5 years of age, with a median age of 3 years old.

**Features**

- abdominal mass (most common presenting feature)
- painless haematuria
- flank pain
- other features: anorexia, fever
- unilateral in 95% of cases
- metastases are found in 20% of patients (most commonly lung)

**Associations**

- Beckwith-Wiedemann syndrome
- as part of WAGR syndrome with Aniridia, Genitourinary malformations, mental Retardation
- hemihypertrophy
- around one-third of cases are associated with a mutation in the WT1 gene on chromosome 11

**Management**

- nephrectomy
- chemotherapy
- radiotherapy if advanced disease
- prognosis: good, 80% cure rate



Which one of the following factors is most likely to invalidate the use of the Modification of Diet in Renal Disease (MDRD) equation to calculate a patient's eGFR?

<input type="radio"/>	A. Diuretic use
<input type="radio"/>	B. Pregnancy
<input type="radio"/>	C. Type 2 diabetes mellitus
<input type="radio"/>	D. Blood pressure of 180/110 mmHg
<input type="radio"/>	E. Female gender

[Next question](#)

GFR tends to increase during pregnancy although the eGFR may not reflect this.

### Chronic kidney disease: eGFR and classification

Serum creatinine may not provide an accurate estimate of renal function due to differences in muscle. For this reason formulas were developed to help estimate the glomerular filtration rate (estimated GFR or eGFR). The most commonly used formula is the Modification of Diet in Renal Disease (MDRD) equation, which uses the following variables:

- serum creatinine
- age
- gender
- ethnicity

Factors which may affect the result

- pregnancy
- muscle mass (e.g. amputees, body-builders)
- eating red meat 12 hours prior to the sample being taken

CKD may be classified according to GFR:

CKD stage	GFR range
1	Greater than 90 ml/min, with some sign of kidney damage on other tests (if all the kidney tests* are normal, there is no CKD)
2	60-90 ml/min with some sign of kidney damage (if kidney tests* are normal, there is no CKD)
3a	45-59 ml/min, a moderate reduction in kidney function
3b	30-44 ml/min, a moderate reduction in kidney function
4	15-29 ml/min, a severe reduction in kidney function
5	Less than 15 ml/min, established kidney failure - dialysis or a kidney transplant may be needed

\*i.e. normal U&Es and no proteinuria

Each one of the following is a cause of sterile pyuria, except:

<input type="radio"/>	A. Renal stones
<input type="radio"/>	B. Membranous glomerulonephritis
<input type="radio"/>	C. Renal tuberculosis
<input type="radio"/>	D. <i>Chlamydia</i>
<input type="radio"/>	E. Appendicitis

Next question

Tubulo-interstitial nephritis may cause sterile pyuria but it is not seen with acute glomerulonephritis

### Sterile pyuria

#### Causes

- partially treated UTI
- urethritis e.g. *Chlamydia*
- renal tuberculosis
- renal stones
- appendicitis
- bladder/renal cell cancer
- adult polycystic kidney disease
- analgesic nephropathy

A 45-year-old presents to the Emergency Department with chest pain. An ECG shows anterior ST elevation and he is thrombolysed with alteplase. His chest pain settles and he is started on aspirin, atorvastatin, bisoprolol and ramipril. Four days later his blood results are as follows:

Urea	22 mmol/l
Creatinine	277 $\mu$ mol/l

What is the most likely cause for the deterioration in renal function?

- ☐ A. Renal artery stenosis
- ☐ B. NSAID related nephropathy
- ☐ C. Statin nephropathy
- ☐ D. Dressler's syndrome
- ☐ E. Haemorrhage into renal cyst

Next question

Flash pulmonary oedema, U&Es worse on ACE inhibitor, asymmetrical kidneys --> renal artery stenosis - do MR angiography

There is likely underlying renal artery stenosis revealed by the addition of an ACE inhibitor. Risk factors such as hypertension and hyperlipidaemia which have contributed to the development of his ischaemic heart disease also put him at risk of renal vascular disease

### Renal vascular disease

Renal vascular disease is most commonly due to atherosclerosis (> 95% of patients). It is associated with risk factors such as smoking and hypertension that cause atheroma elsewhere in the body. It may present as hypertension, chronic renal failure or 'flash' pulmonary oedema. In younger patients however fibromuscular dysplasia (FMD) needs to be considered. FMD is more common in young women and characteristically has a 'string of beads' appearance on angiography. Patients respond well to balloon angioplasty

### Investigation

- MR angiography is now the investigation of choice
- CT angiography
- conventional renal angiography is less commonly performed used nowadays, but may still have a role when planning surgery

**Question 69 of 93**

Next

A 24-year-old man who has a sister with adult polycystic kidney disease (ADPKD) asks if he could be screened for the disease. What is the most appropriate screening test?

- ☐ A. PKD1 gene testing
- ☐ B. CT abdomen
- ☐ C. Urine microscopy
- ☐ D. Ultrasound abdomen
- ☐ E. Anti-polycystin 1 antibodies levels

Next question

Ultrasound is the screening test for adult polycystic kidney disease

Genetic testing is still not routinely recommended for screening family members. Sensitivity for ADPKD1 is 99% for at-risk patients older than 20 years

**ADPKD**

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	ADPKD type 2
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

Alport's syndrome is due to a defect in:

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Fibrillin-2      |
| <input type="radio"/> | B. Type II collagen |
| <input type="radio"/> | C. Fibrillin-1      |
| <input type="radio"/> | D. Type IV collagen |
| <input type="radio"/> | E. Type V collagen  |

Next question

Alport's syndrome - type IV collagen defect

### Alport's syndrome

Alport's syndrome is usually inherited in an X-linked dominant pattern\*. It is due to a defect in the gene which codes for type IV collagen resulting in an abnormal glomerular-basement membrane (GBM). The disease is more severe in males with females rarely developing renal failure

A favourite question is an Alport's patient with a failing renal transplant. This may be caused by the presence of anti-GBM antibodies leading to a Goodpasture's syndrome like picture

Alport's syndrome usually presents in childhood. The following features may be seen:

- microscopic haematuria
- progressive renal failure
- bilateral sensorineural deafness
- lenticonus: protrusion of the lens surface into the anterior chamber
- retinitis pigmentosa

\*in around 85% of cases - 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants existing

What is the most likely outcome following the diagnosis of minimal change nephropathy in a 10-year-old male?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Chronic kidney disease requiring renal replacement therapy within 30 years |
| <input type="radio"/> | B. Full recovery and no further episodes                                      |
| <input type="radio"/> | C. Full recovery but with later relapses                                      |
| <input type="radio"/> | D. Chronic kidney disease not requiring renal replacement therapy             |
| <input type="radio"/> | E. Chronic kidney disease requiring renal replacement therapy within 10 years |

Next question

As 1/3 of patients have infrequent relapses and 1/3 of patients have frequent relapses a majority (2/3) will have later recurrent episodes. It is important however to stress to patients that generally speaking the longer term prognosis in minimal change glomerulonephritis is good.

### Minimal change glomerulonephritis

Minimal change glomerulonephritis nearly always presents as nephrotic syndrome, accounting for 75% of cases in children and 25% in adults

The majority of cases are idiopathic, but in around 10-20% a cause is found:

- drugs: NSAIDs, rifampicin
- Hodgkin's lymphoma, thymoma
- infectious mononucleosis

### Features

- nephrotic syndrome
- normotension - hypertension is rare
- highly selective proteinuria\*
- renal biopsy: electron microscopy shows fusion of podocytes

### Management

- majority of cases (80%) are steroid responsive
- cyclophosphamide is the next step for steroid resistant cases

Prognosis is overall good, although relapse is common. Roughly:

- 1/3 have just one episode
- 1/3 have infrequent relapses
- 1/3 have frequent relapses which stop before adulthood

\*only intermediate-sized proteins such as albumin and transferrin leak through the glomerulus

Which one of the following statements regarding minimal change glomerulonephritis is incorrect?

<input type="radio"/>	A. Has a good prognosis
<input type="radio"/>	B. The majority of cases are steroid responsive
<input type="radio"/>	C. Is a common cause of nephrotic syndrome
<input type="radio"/>	D. Hypertension is found in approximately 25% of patients
<input type="radio"/>	E. Haematuria is rare

Next question

Hypertension and haematuria are rare in minimal change glomerulonephritis

### Minimal change glomerulonephritis

Minimal change glomerulonephritis nearly always presents as nephrotic syndrome, accounting for 75% of cases in children and 25% in adults

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- highly selective proteinuria\*
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- 1/3 have frequent relapses which stop before adulthood

\*only intermediate-sized proteins such as albumin and transferrin leak through the glomerulus

**Question 73 of 93**

Next

A 65-year-old man presents to the Emergency Department with lethargy and leg swelling. Initial bloods show the following:

Na+	138 mmol/l
K+	5.6 mmol/l
Urea	19.3 mmol/l
Creatinine	299 µmol/l

His renal function six months ago was normal. Which one of his regular medications is it most important to stop straight away?

- ☐ A. Ibuprofen
- ☐ B. Warfarin
- ☐ C. Paracetamol
- ☐ D. Diazepam
- ☐ E. Atenolol

NSAIDs such as ibuprofen can significantly worsen renal impairment and must be avoided in patients with acute kidney injury or chronic kidney disease.

**Prescribing in patients with renal failure**

Questions regarding which drugs to avoid in renal failure are common

Drugs to avoid in renal failure

- antibiotics: tetracycline, nitrofurantoin
- NSAIDs
- lithium
- metformin

Drugs likely to accumulate in chronic kidney disease - need dose adjustment

- most antibiotics including penicillins, cephalosporins, vancomycin, gentamicin, streptomycin
- digoxin, atenolol
- methotrexate
- sulphonylureas
- furosemide
- opioids

Drugs relatively safe - can sometimes use normal dose depending on the degree of chronic kidney disease

- antibiotics: erythromycin, rifampicin
- diazepam
- warfarin



A 67-year-old with chronic kidney disease stage 4 and metastatic prostate cancer presents as his pain is not controlled with co-codamol. Which one of the following opioids is it most appropriate to use given his impaired renal function?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Buprenorphine |
| <input type="radio"/> | B. Morphine      |
| <input type="radio"/> | C. Hydromorphone |
| <input type="radio"/> | D. Diamorphine   |
| <input type="radio"/> | E. Tramadol      |

[Next question](#)

Alfentanil, buprenorphine and fentanyl are the preferred opioids in patients with chronic kidney disease.

### Palliative care prescribing: pain

#### NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

#### Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered

#### SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

## Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

## Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

## Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted. NICE give the following advice on conversion:

- a transdermal fentanyl 12 microgram patch equates to approximately 45 mg oral morphine daily
- a transdermal buprenorphine 20 microgram patch equates to approximately 30 mg oral morphine daily.

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

Which one of the following statements is true regarding autosomal recessive polycystic kidney disease?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Onset is typically in the third decade                        |
| <input type="radio"/> | B. Liver involvement is rare                                     |
| <input type="radio"/> | C. Is due to a defect on chromosome 16                           |
| <input type="radio"/> | D. More common than autosomal dominant polycystic kidney disease |
| <input type="radio"/> | E. May be diagnosed on prenatal ultrasound                       |

Next question

### ARPKD

Autosomal recessive polycystic kidney disease (ARPKD) is much less common than autosomal dominant disease (ADPKD). It is due to a defect in a gene located on chromosome 6

Diagnosis may be made on prenatal ultrasound or in early infancy with abdominal masses and renal failure. End-stage renal failure develops in childhood. Patients also typically have liver involvement, for example portal and interlobular fibrosis

A 12-year-old boy is investigated for a purpuric rash on the extensor surfaces of his lower legs. He also has a history of abdominal pain and an urticarial rash. The following results are obtained:

Urine dipstick:	blood ++
-----------------	----------

What would be the likely finding on renal biopsy?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Linear IgG deposits             |
| <input type="radio"/> | B. No change                       |
| <input type="radio"/> | C. Sclerosis within the glomerulus |
| <input type="radio"/> | D. Mesangial hypercellularity      |
| <input type="radio"/> | E. Basement membrane thickening    |

Next question

Henoch-Schonlein purpura is associated with IgA nephropathy

### Henoch-Schonlein purpura

Henoch-Schonlein purpura (HSP) is an IgA mediated small vessel vasculitis. There is a degree of overlap with IgA nephropathy (Berger's disease). HSP is usually seen in children following an infection

#### Features

- palpable purpuric rash (with localized oedema) over buttocks and extensor surfaces of arms and legs
- abdominal pain
- polyarthrititis
- features of IgA nephropathy may occur e.g. haematuria, renal failure

#### Treatment

- analgesia for arthralgia
- treatment of nephropathy is generally supportive. There is inconsistent evidence for the use of steroids and immunosuppressants

#### Prognosis

- usually excellent, HSP is a self-limiting condition, especially in children without renal involvement
- around 1/3rd of patients have a relapse

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Next

You are asked to review a 75-year-old female on the surgical wards due to hyperkalaemia. Results are as follows:

	Plasma	Urine
Na <sup>+</sup> (mmol/l)	129	5
K <sup>+</sup> (mmol/l)	6.8	
Urea (mmol/l)	26	350
Creatinine (μmol/l)	262	
Osmolality (mosmol/kg)	296	470

What is the most likely diagnosis?

- ☐ A. Acute tubular necrosis
- ☐ B. Hyperosmolar non-ketotic coma
- ☐ C. Hydronephrosis
- ☐ D. Prerenal uraemia
- ☐ E. Pyelonephritis

ATN or prerenal uraemia? In prerenal uraemia think of the kidneys holding on to sodium to preserve volume

The low urine sodium points towards prerenal uraemia, as does the urine:plasma osmolality and urea ratio

## Acute renal failure: acute tubular necrosis vs. Prerenal uraemia

Prerenal uraemia - kidneys hold on to sodium to preserve volume

	Pre-renal uraemia	Acute tubular necrosis
Urine sodium	< 20 mmol/L	> 30 mmol/L
Fractional sodium excretion*	< 1%	> 1%
Fractional urea excretion**	< 35%	> 35%
Urine:plasma osmolality	> 1.5	< 1.1
Urine:plasma urea	> 10:1	< 8:1
Specific gravity	> 1020	< 1010
Urine	'bland' sediment	brown granular casts
Response to fluid challenge	Yes	No

\*fractional sodium excretion = (urine sodium/plasma sodium) / (urine creatinine/plasma creatinine) x 100

\*\*fractional urea excretion = (urine urea /blood urea ) / (urine creatinine/plasma creatinine) x 100

Which of the following types of renal stones are said to have a semi-opaque appearance on x-ray?

- ☐ A. Calcium oxalate
- ☐ B. Cystine stones
- ☐ C. Urate stones
- ☐ D. Xanthine stones
- ☐ E. Triple phosphate stones

Next question

#### Renal stones on x-ray

- cystine stones: semi-opaque
- urate + xanthine stones: radio-lucent

#### Renal stones: imaging

The table below summarises the appearance of different types of renal stone on x-ray

Type	Frequency	Radiograph appearance
Calcium oxalate	40%	Opaque
Mixed calcium oxalate/phosphate stones	25%	Opaque
Triple phosphate stones*	10%	Opaque
Calcium phosphate	10%	Opaque
Urate stones	5-10%	Radio-lucent
Cystine stones	1%	Semi-opaque, 'ground-glass' appearance
Xanthine stones	<1%	Radio-lucent

\*stag-horn calculi involve the renal pelvis and extend into at least 2 calyces. They develop in alkaline urine and are composed of struvite (ammonium magnesium phosphate, triple phosphate). *Ureaplasma urealyticum* and *Proteus* infections predispose to their formation

A 65-year-old man who is known to have colorectal cancer is referred to the renal clinic. His GP performed a protein-creatinine ratio as he had been complaining of 'frothy' urine. The results suggest nephrotic range proteinuria which is confirmed on a 24-hour urinary collection. Assuming the proteinuria is related to his colorectal cancer what is the renal histology most likely to show?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Mesangiocapillary glomerulonephritis     |
| <input type="radio"/> | B. Minimal change glomerulonephritis        |
| <input type="radio"/> | C. Focal segmental glomerulosclerosis       |
| <input type="radio"/> | D. Membranous glomerulonephritis            |
| <input type="radio"/> | E. Membranoproliferative glomerulonephritis |

[Next question](#)

Nephrotic syndrome - malignancies cause membranous glomerulonephritis

Patients with underlying malignancies such as lung, colon and gastric cancer may develop nephrotic syndrome as a paraneoplastic complication. This appears to be an association with HLA-DR3.

Lymphomas tend to be associated with minimal change disease.

### Nephrotic syndrome: causes

Primary glomerulonephritis accounts for around 80% of cases

- minimal change glomerulonephritis (causes 80% in children, 30% in adults)
- membranous glomerulonephritis
- focal segmental glomerulosclerosis
- membranoproliferative glomerulonephritis

Systemic disease (about 20%)

- diabetes mellitus
- systemic lupus erythematosus
- amyloidosis

Drugs

- gold (sodium aurothiomalate), penicillamine

Others

- congenital
- neoplasia: carcinoma, lymphoma, leukaemia, myeloma
- infection: bacterial endocarditis, hepatitis B, malaria

**Question 80 of 93**

Next

A 65-year-old man is seen in the Emergency Department complaining of muscle weakness and lethargy. Admission bloods show the following:

Na <sup>+</sup>	138 mmol/l
K <sup>+</sup>	6.3 mmol/l
Bicarbonate	15 mmol/l
Urea	9.2 mmol/l
Creatinine	110 µmol/l

What is the most appropriate initial treatment to lower the serum potassium level?

- ☐ A. Intravenous bicarbonate
- ☐ B. Haemodialysis
- ☒ C. Insulin/dextrose infusion
- ☐ D. Intravenous calcium gluconate
- ☐ E. Oral calcium resonium

Next question

Calcium gluconate would stabilise the myocardium but would not reduce the serum potassium level.

**Hyperkalaemia: management**

Untreated hyperkalaemia may cause life-threatening arrhythmias. Precipitating factors should be addressed (e.g. acute renal failure) and aggravating drugs stopped (e.g. ACE inhibitors). Management may be categorised by the aims of treatment

Stabilisation of the cardiac membrane

- intravenous calcium gluconate

Short-term shift in potassium from extracellular to intracellular fluid compartment

- combined insulin/dextrose infusion
- nebulised salbutamol

Removal of potassium from the body

- calcium resonium (orally or enema)
- loop diuretics
- dialysis



### Question 81 of 93

Next

A patient develops mesangiocapillary glomerulonephritis secondary to partial lipodystrophy. Which type of complement is likely to be low?

<input type="radio"/>	A. C3
<input type="radio"/>	B. C4
<input type="radio"/>	C. C2
<input type="radio"/>	D. C9
<input type="radio"/>	E. C6

Next question

#### Mesangiocapillary glomerulonephritis (membranoproliferative)

- type 1: cryoglobulinaemia, hepatitis C
- type 2: partial lipodystrophy

#### Mesangiocapillary glomerulonephritis

##### Overview

- also known as membranoproliferative glomerulonephritis
- may present as nephrotic syndrome, haematuria or proteinuria
- poor prognosis

##### Type 1

- subendothelial immune deposits
- cause: cryoglobulinaemia, hepatitis C

##### Type 2 - 'dense deposit disease'

- intramembranous deposits of electron dense material
- causes: partial lipodystrophy, factor H deficiency
- reduced serum complement
- C3b nephritic factor (an antibody against C3bBb) found in 70%

##### Type 3

- causes: hepatitis B and C

##### Management

- steroids may be effective

**Question 82 of 93**

Next

A 45-year-old woman with type 1 diabetes mellitus is reviewed in the diabetes clinic. Three months ago her blood tests were as followed:

K <sup>+</sup>	4.5 mmol/l
Creatinine	116 µmol/l
eGFR	47 ml/min

At the time she was started on lisinopril to treat both the hypertension and act as a renoprotective agent. Lisinopril had been titrated up to treatment dose. Her current bloods are as follows:

K <sup>+</sup>	4.9 mmol/l
Creatinine	123 µmol/l
eGFR	44 ml/min

Of the following options, what is the most appropriate course of action?

- ☐ A. Stop lisinopril and arrange investigations to exclude renal artery stenosis
- ☐ B. Switch to an angiotensin 2 receptor blocker
- ☐ C. Switch to a different ACE inhibitor
- ☐ D. No action
- ☐ E. Reduce dose of lisinopril

Next question

The small change in both the creatinine and eGFR are acceptable and below the threshold where ACE inhibitors should be stopped

**Chronic kidney disease: hypertension**

The majority of patients with chronic kidney disease (CKD) will require more than two drugs to treat hypertension. ACE inhibitors are first line and are particularly helpful in proteinuric renal disease (e.g. diabetic nephropathy). As these drugs tend to reduce filtration pressure a small fall in glomerular filtration pressure (GFR) and rise in creatinine can be expected. NICE suggest that a decrease in eGFR of up to 25% or a rise in creatinine of up to 30% is acceptable, although any rise should prompt careful monitoring and exclusion of other causes (e.g. NSAIDs). A rise greater than this may indicate underlying renovascular disease.

Furosemide is useful as an anti-hypertensive in patients with CKD, particularly when the GFR falls to below 45 ml/min\*. It has the added benefit of lowering serum potassium. High doses are usually required. If the patient becomes at risk of dehydration (e.g. Gastroenteritis) then consideration should be given to temporarily stopping the drug

\*the NKF K/DOQI guidelines suggest a lower cut-off of less than 30 ml/min

Which one of the following may be useful in the prevention of oxalate renal stones?

<input type="radio"/>	A. Ferrous sulphate
<input type="radio"/>	B. Thiazide diuretics
<input type="radio"/>	C. Lithium
<input type="radio"/>	D. Pyridoxine
<input type="radio"/>	E. Allopurinol

Next question

## Renal stones: management

### Acute management of renal colic

Diclofenac 75 mg by intramuscular injection is the analgesia of choice for renal colic\*. A second dose can be given after 30 minutes if necessary

### Prevention of renal stones

#### Calcium stones

- high fluid intake
- low animal protein, low salt diet (a low calcium diet has not been shown to be superior to a normocalcaemic diet)
- thiazide diuretics (increase distal tubular calcium resorption)
- stones < 5 mm will usually pass spontaneously
- lithotripsy, nephrolithotomy may be required

#### Oxalate stones

- cholestyramine reduces urinary oxalate secretion
- pyridoxine reduces urinary oxalate secretion

#### Uric acid stones

- allopurinol
- urinary alkalinization e.g. oral bicarbonate

\*PR diclofenac is an alternative

**Question 84 of 93**

Next

A 10-year-old boy is admitted to hospital with diarrhoea and lethargy. There is a known local outbreak of E coli O157:H7 and his initial bloods show evidence of acute renal failure. Given the likely diagnosis, which one of the following investigation results would be expected?

<input type="radio"/>	A. Increased prothrombin time
<input type="radio"/>	B. Thrombocytosis
<input type="radio"/>	C. Fragmented red blood cells
<input type="radio"/>	D. Right-shift of the white blood cells
<input type="radio"/>	E. Raised serum haptoglobins

Next question

Serum haptoglobins (which bind haemoglobin) and the platelet count are decreased in haemolytic uraemic syndrome.

**Haemolytic uraemic syndrome**

Haemolytic uraemic syndrome is generally seen in young children and produces a triad of:

- acute renal failure
- microangiopathic haemolytic anaemia
- thrombocytopenia

**Causes**

- post-dysentery - classically E coli O157:H7 ('verotoxigenic', 'enterohaemorrhagic')
- tumours
- pregnancy
- ciclosporin, the Pill
- systemic lupus erythematosus
- HIV

**Investigations**

- full blood count: anaemia, thrombocytopenia, fragmented blood film
- U&E: acute renal failure
- stool culture

**Management**

- treatment is supportive e.g. Fluids, blood transfusion and dialysis if required
- there is no role for antibiotics, despite the preceding diarrhoeal illness in many patients
- the indications for plasma exchange in HUS are complicated. As a general rule plasma exchange is reserved for severe cases of HUS not associated with diarrhoea

Which one of the following is not a risk factor for the development of calcium oxalate and calcium phosphate renal stones?

<input type="radio"/>	A. Bendroflumethiazide
<input type="radio"/>	B. Aminophylline
<input type="radio"/>	C. Acetazolamide
<input type="radio"/>	D. Furosemide
<input type="radio"/>	E. Prednisolone

Next question

Bendroflumethiazide may help prevent the formation of calcium based renal stones. It may however theoretically increase the risk of urate based stones

### Renal stones: risk factors

#### Risk factors

- dehydration
- hypercalciuria, hyperparathyroidism, hypercalcaemia
- cystinuria
- high dietary oxalate
- renal tubular acidosis
- medullary sponge kidney, polycystic kidney disease
- beryllium or cadmium exposure

#### Risk factors for urate stones

- gout
- ileostomy: loss of bicarbonate and fluid results in acidic urine, causing the precipitation of uric acid

#### Drug causes

- drugs that promote calcium stones: loop diuretics, steroids, acetazolamide, theophylline
- thiazides can prevent calcium stones (increase distal tubular calcium resorption)

**Question 86 of 93**

Next

A 34-year-old man who has injected heroin for the past 10 years is admitted to the Emergency Department. You notice on the computer that his serum creatinine has been slowly rising over recent years. His latest results show the following:

Na <sup>+</sup>	140 mmol/l
K <sup>+</sup>	4.8 mmol/l
Bicarbonate	26 mmol/l
Urea	8.1 mmol/l
Creatinine	156 µmol/l

Urine dipstick	Protein ++, nil else
----------------	----------------------

What is the most likely cause of his deteriorating renal function?

- ☐ A. Focal segmental glomerulosclerosis
- ☐ B. Amyloidosis
- ☐ C. Mesangiocapillary glomerulonephritis
- ☐ D. Chronic pyelonephritis
- ☐ E. Renal vein thrombosis

Next question

Heroin is a known cause of focal segmental glomerulosclerosis.

**Focal segmental glomerulosclerosis**

Focal segmental glomerulosclerosis is cause of nephrotic syndrome and chronic kidney disease. It generally presents in young adults.

**Causes**

- idiopathic
- secondary to other renal pathology e.g. IgA nephropathy, reflux nephropathy
- HIV
- heroin
- Alport's syndrome
- sickle-cell

Focal segmental glomerulosclerosis is noted for having a high recurrence rate in renal transplants

**Question 87 of 93**

Next

A 43-year-old is referred to the renal clinic after presenting with peripheral oedema. He has no past medical history of note. Routine bloods ordered by his GP showed the following:

Hb	14.1 g/dl
Platelets	$199 \times 10^9/l$
WBC	$5.6 \times 10^9/l$

Na <sup>+</sup>	141 mmol/l
K <sup>+</sup>	4.8 mmol/l
Urea	8.3 mmol/l
Creatinine	143 $\mu$ mol/l

Bilirubin	21 $\mu$ mol/l
ALP	84 u/l
ALT	22 u/l
$\gamma$ GT	33 u/l
Albumin	26 g/l

His urinary protein is 4.2g/24 hours. On examination in the clinic he has pitting oedema of the ankles and his blood pressure is 160/92 mmHg. A renal biopsy is ordered and reported as follows:

**Light microscopy**

Mesangium: normal, with no hypercellularity. The capillary walls are thickened. Subepithelial deposits are seen.

Given the likely diagnosis, which one of the following drugs is most likely to be beneficial?

- ☐ A. ACE inhibitor
- ☐ B. Ciclosporin
- ☐ C. Corticosteroid
- ☐ D. Aspirin
- ☐ E. Cyclophosphamide

Next question

This patient has membranous glomerulonephritis. The history is typical with a middle-aged man presenting with nephrotic syndrome and characteristic biopsy findings.

Corticosteroids by themselves have not been shown to be effective in membranous glomerulonephritis. ACE inhibitors have however been shown to reduce proteinuria.

## **Membranous glomerulonephritis**

Membranous glomerulonephritis is the commonest type of glomerulonephritis in adults and is the third most common cause of end-stage renal failure (ESRF). It usually presents with nephrotic syndrome or proteinuria.

Renal biopsy demonstrates:

- sub-epithelial immune complex (mainly IgG and C3) deposition in the glomerulus
- electron microscopy: the basement membrane is thickened with sub-epithelial electron dense deposits

### Causes

- idiopathic
- infections: hepatitis B, malaria
- malignancy: lung cancer, lymphoma, leukaemia
- drugs: gold, penicillamine, NSAIDs
- systemic lupus erythematosus (class V disease)

### Prognosis - rule of thirds

- one-third: spontaneous remission
- one-third: remain proteinuric
- one-third: develop ESRF

### Management

- immunosuppression: corticosteroids alone have not been shown to be effective. A combination of corticosteroid + another agent such as chlorambucil is often used
- blood pressure control: ACE inhibitors have been shown to reduce proteinuria
- consider anticoagulation



A 29-year-old man has his renal function checked. The eGFR is calculated to be 54 ml/min. Which one of the following factors is most likely to explain this unexpectedly low result?

- ☐ A. Drinking a large amount of milk
- ☐ B. Being dehydrated when the blood sample was taken
- ☐ C. Being very tall
- ☐ D. Excessive alcohol intake
- ☐ E. Large muscle mass secondary to body building

The eGFR is often inaccurate in people with extremes of muscle mass. Body builders often have an inappropriately low eGFR.

### Chronic kidney disease: eGFR and classification

Serum creatinine may not provide an accurate estimate of renal function due to differences in muscle. For this reason formulas were developed to help estimate the glomerular filtration rate (estimated GFR or eGFR). The most commonly used formula is the Modification of Diet in Renal Disease (MDRD) equation, which uses the following variables:

- serum creatinine
- age
- gender
- ethnicity

Factors which may affect the result

- pregnancy
- muscle mass (e.g. amputees, body-builders)
- eating red meat 12 hours prior to the sample being taken

CKD may be classified according to GFR:

CKD stage	GFR range
1	Greater than 90 ml/min, with some sign of kidney damage on other tests (if all the kidney tests* are normal, there is no CKD)
2	60-90 ml/min with some sign of kidney damage (if kidney tests* are normal, there is no CKD)
3a	45-59 ml/min, a moderate reduction in kidney function
3b	30-44 ml/min, a moderate reduction in kidney function
4	15-29 ml/min, a severe reduction in kidney function
5	Less than 15 ml/min, established kidney failure - dialysis or a kidney transplant may be needed

\*i.e. normal U&Es and no proteinuria

### Question 89 of 93

Which one of the following is associated with a better prognosis in patients with IgA nephropathy?

<input type="radio"/>	A. Heavy proteinuria at presentation
<input type="radio"/>	B. Male gender
<input type="radio"/>	C. Hyperlipidaemia
<input type="radio"/>	D. Frank haematuria
<input type="radio"/>	E. ACE genotype DD

[Next question](#)

## IgA nephropathy

### Basics

- also called Berger's disease or mesangioproliferative glomerulonephritis
- commonest cause of glomerulonephritis worldwide
- pathogenesis unknown, ?mesangial deposition of IgA immune complexes
- histology: mesangial hypercellularity, positive immunofluorescence for IgA & C3

### Differentiating between IgA nephropathy and post-streptococcal glomerulonephritis

- post-streptococcal glomerulonephritis is associated with low complement levels
- main symptom in post-streptococcal glomerulonephritis is proteinuria (although haematuria can occur)
- there is typically an interval between URTI and the onset of renal problems in post-streptococcal glomerulonephritis

### Presentations

- young male, recurrent episodes of macroscopic haematuria
- typically associated with mucosal infections e.g., URTI
- nephrotic range proteinuria is rare
- renal failure

### Associated conditions

- alcoholic cirrhosis
- coeliac disease/dermatitis herpetiformis

## Management

- steroids/immunosuppressants not be shown to be useful

## Prognosis

- 25% of patients develop ESRF
- markers of good prognosis: frank haematuria
- markers of poor prognosis: male gender, proteinuria (especially > 2 g/day), hypertension, smoking, hyperlipidaemia, ACE genotype DD

**Question 90 of 93**[Next](#)

Autosomal dominant polycystic kidney disease type 2 is associated with a gene defect in:

- ☐ A. Chromosome 4
- ☐ B. Chromosome 8
- ☐ C. Chromosome 12
- ☐ D. Chromosome 16
- ☐ E. Chromosome 20

[Next question](#)

ADPKD type 2 = chromosome 4 = 15% of cases

**ADPKD**

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	ADPKD type 2
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

**Question 91 of 93**

Next

Which of the following factors would suggest that a patient has pre-renal uraemia rather than established acute tubular necrosis?

- ☐ A. Urine sodium = 70 mmol/L
- ☐ B. Fractional urea excretion = 20%
- ☐ C. No response to fluid challenge
- ☐ D. Urine:plasma urea ratio 5:1
- ☐ E. Specific gravity = 1005

Next question

ATN or prerenal uraemia? In prerenal uraemia think of the kidneys holding on to sodium to preserve volume

**Acute renal failure: acute tubular necrosis vs. Prerenal uraemia**

Prerenal uraemia - kidneys hold on to sodium to preserve volume

	Pre-renal uraemia	Acute tubular necrosis
Urine sodium	< 20 mmol/L	> 30 mmol/L
Fractional sodium excretion*	< 1%	> 1%
Fractional urea excretion**	< 35%	> 35%
Urine:plasma osmolality	> 1.5	< 1.1
Urine:plasma urea	> 10:1	< 8:1
Specific gravity	> 1020	< 1010
Urine	'bland' sediment	brown granular casts
Response to fluid challenge	Yes	No

\*fractional sodium excretion = (urine sodium/plasma sodium) / (urine creatinine/plasma creatinine) x 100

\*\*fractional urea excretion = (urine urea /blood urea ) / (urine creatinine/plasma creatinine) x 100

**Question 92 of 93**[Next](#)

A 63-year-old man is admitted with severe right sided loin pain to the Emergency Department. A urine dipstick shows blood +++, leucocytes +, protein +. An abdominal radiograph is therefore ordered which shows a stag-horn calculus in the right renal pelvis. What are stag-horn calculi normally composed of?

- ☐ A. Xanthine
- ☐ B. Magnesium ammonium phosphate
- ☐ C. Calcium oxalate
- ☐ D. Uric acid
- ☐ E. Magnesium calcium phosphate

[Next question](#)**Stag-horn calculi**

- composed of **Struvite** (ammonium magnesium phosphate, triple phosphate)
- form in alkaline urine (ammonia producing bacteria such as *Ureaplasma urealyticum* and *Proteus* therefore predispose)

**Renal stones: imaging**

The table below summarises the appearance of different types of renal stone on x-ray

Type	Frequency	Radiograph appearance
Calcium oxalate	40%	Opaque
Mixed calcium oxalate/phosphate stones	25%	Opaque
Triple phosphate stones*	10%	Opaque
Calcium phosphate	10%	Opaque
Urate stones	5-10%	Radio-lucent
Cystine stones	1%	Semi-opaque, 'ground-glass' appearance
Xanthine stones	<1%	Radio-lucent

\*stag-horn calculi involve the renal pelvis and extend into at least 2 calyces. They develop in alkaline urine and are composed of struvite (ammonium magnesium phosphate, triple phosphate). *Ureaplasma urealyticum* and *Proteus* infections predispose to their formation

### Question 93 of 93

Which one of the following is the most common type of SLE associated renal disease?

<input type="radio"/>	A.	Class II: mesangial glomerulonephritis
<input type="radio"/>	B.	Class III: focal (and segmental) proliferative glomerulonephritis
<input type="radio"/>	C.	Class IV: diffuse proliferative glomerulonephritis
<input type="radio"/>	D.	Class V: diffuse membranous glomerulonephritis
<input type="radio"/>	E.	Class VI: sclerosing glomerulonephritis

Diffuse proliferative glomerulonephritis is the most common and severe form of renal disease in SLE patients

### SLE: renal complications

WHO classification

- class I: normal kidney
- class II: mesangial glomerulonephritis
- class III: focal (and segmental) proliferative glomerulonephritis
- class IV: diffuse proliferative glomerulonephritis
- class V: diffuse membranous glomerulonephritis
- class VI: sclerosing glomerulonephritis

Class IV (diffuse proliferative glomerulonephritis) is the most common and severe form

Management

- treat hypertension
- corticosteroids if clinical evidence of disease
- immunosuppressants e.g. azathiopine/cyclophosphamide

A 27-year-old man presents to the Emergency Department with 2 day history of severe headache and pyrexia (38.2°C). A CT scan is reported as follows:

**CT: Brain**

Petechial haemorrhages in the temporal and inferior frontal lobes. No mass effect. Brain parenchyma otherwise normal

What is the most likely diagnosis?

<input type="radio"/>	A. Brain abscess
<input type="radio"/>	B. Meningococcal meningitis
<input type="radio"/>	C. Cerebral malaria
<input type="radio"/>	D. Herpes simplex encephalitis
<input type="radio"/>	E. New variant CJD

Next question

CT head showing temporal lobe changes - think herpes simplex encephalitis

**Herpes simplex encephalitis**

Herpes simplex (HSV) encephalitis is a common topic in the exam. The virus characteristically affects the temporal lobes - questions may give the result of imaging or describe temporal lobe signs e.g. aphasia

**Features**

- fever, headache, psychiatric symptoms, seizures, vomiting
- focal features e.g. aphasia
- peripheral lesions (e.g. cold sores) have no relation to presence of HSV encephalitis

**Pathophysiology**

- HSV-1 responsible for 95% of cases in adults
- typically affects temporal and inferior frontal lobes

**Investigation**

- CSF: lymphocytosis, elevated protein



- PCR for HSV
- CT: medial temporal and inferior frontal changes (e.g. petechial haemorrhages) - normal in one-third of patients
- MRI is better
- EEG pattern: lateralised periodic discharges at 2 Hz

#### Treatment

- intravenous aciclovir

The prognosis is dependent on whether aciclovir is commenced early. If treatment is started promptly the mortality is 10-20%. Left untreated the mortality approaches 80%

## Question 2 of 204

Next

A 29-year-old man presents complaining of visual disturbance. Examination reveals a right superior homonymous quadrantanopia. Where is the lesion most likely to be?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Optic chiasm        |
| <input type="radio"/> | B. Left temporal lobe  |
| <input type="radio"/> | C. Right temporal lobe |
| <input type="radio"/> | D. Left optic nerve    |
| <input type="radio"/> | E. Left parietal lobe  |

Next question

Visual field defects:

- left homonymous hemianopia means visual field defect to the left, i.e. lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

### Visual field defects

The main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

A congruous defect simply means complete or symmetrical visual field loss and conversely an incongruous defect is incomplete or asymmetric. Please see the link for an excellent diagram.

Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias\*

- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe

- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

#### Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

\*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details:

<http://www.ncbi.nlm.nih.gov/pubmed/9109741>

A 64-year-old man with a history of Parkinson's disease is reviewed in clinic and a decision has been made to start him on cabergoline. Which one of the following adverse effects is most strongly associated with this drug?

<input type="radio"/>	A. Optic neuritis
<input type="radio"/>	B. Transient rise in liver function tests
<input type="radio"/>	C. Pulmonary fibrosis
<input type="radio"/>	D. Renal failure
<input type="radio"/>	E. Thrombocytopenia

[Next question](#)

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline

- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

#### Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

#### COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

#### Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benztropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

#### Question 4 of 204

Next

A 76-year-old man is admitted with a right hemiparesis. He first noticed weakness on his right side around six hours ago. A CT scan shows an ischaemic stroke and aspirin 300mg is commenced. terms of further management in the acute phase, which one of the following values should not be corrected?

<input type="radio"/>	A. BP 210/110
<input type="radio"/>	B. Blood glucose 11.2 mmol/l
<input type="radio"/>	C. Oxygen saturation 93%
<input type="radio"/>	D. Temp 38.3°C
<input type="radio"/>	E. Blood glucose 3.5 mmol/l

Next question

Hypertension should not be treated in the initial period following a stroke

Elevated blood pressure should not be treated in the acute phase following a stroke unless complications develop. Other physiological parameters should be kept within normal limits - an aggressive approach with respect to this has been shown to improve outcome

#### Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued stroke guidelines in 2008, although they modified their guidance with respect to antiplatelet therapy in 2010.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy\*
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commenced on a statin. Many physicians will delay treatment until after at least 48 hours due to the risk of haemorrhagic transformation

#### Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 hours\*\* of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

## Secondary prevention

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- clopidogrel is now recommended by NICE ahead of combination use of aspirin plus modified release (MR) dipyridamole in people who have had an ischaemic stroke
- aspirin plus MR dipyridamole is now recommended after an ischaemic stroke only if clopidogrel is contraindicated or not tolerated, but treatment is no longer limited to 2 years' duration
- MR dipyridamole alone is recommended after an ischaemic stroke only if aspirin or clopidogrel are contraindicated or not tolerated, again with no limit on duration of treatment

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST\*\*\* criteria or > 50% according to NASCET\*\*\*\* criteria

\*the 2009 Controlling hypertension and hypotension immediately post-stroke (CHHIPS) trial may change thinking on this but guidelines have yet to change to reflect this

\*\*SIGN recommend a window of 4.5 hours

\*\*\*European Carotid Surgery Trialists' Collaborative Group

\*\*\*\*North American Symptomatic Carotid Endarterectomy Trial

A 23-year-old man is referred to neurology clinic. He describes episodes of leg weakness following bouts of laughing whilst out with friends. The following weekend his friends described a brief collapse following a similar episode. What is the most likely diagnosis?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Stokes-Adams attack             |
| <input type="radio"/> | B. Cataplexy                       |
| <input type="radio"/> | C. Hypokalaemic periodic paralysis |
| <input type="radio"/> | D. Absence seizure                 |
| <input type="radio"/> | E. Myasthenia gravis               |

[Next question](#)

### Cataplexy

Cataplexy describes the sudden and transient loss of muscular tone caused by strong emotion (e.g. laughter, being frightened). Around two-thirds of patients with narcolepsy have cataplexy.

Features range from buckling knees to collapse.



A 44-year-old woman presents with pain in her right hand and forearm which has been getting worse for the past few weeks. There is no history of trauma. The pain is concentrated around the thumb and index finger and is often worse at night. Shaking her hand seems to provide some relief. On examination there is weakness of the abductor pollicis brevis and reduced sensation to fine touch at the index finger. What is the most likely diagnosis?

<input type="radio"/>	A. C6 entrapment neuropathy
<input type="radio"/>	B. Thoracic outlet syndrome
<input type="radio"/>	C. Carpal tunnel syndrome
<input type="radio"/>	D. Cervical rib
<input type="radio"/>	E. Pancoast's tumour

[Next question](#)

More proximal symptoms would be expected with a C6 entrapment neuropathy e.g. weakness of the biceps muscle or reduced biceps reflex.

Patients with carpal tunnel syndrome often get relief from shaking their hands and this may be an important clue in exam questions.

### Carpal tunnel syndrome

Carpal tunnel syndrome is caused by compression of median nerve in the carpal tunnel.

#### History

- pain/pins and needles in thumb, index, middle finger
- unusually the symptoms may 'ascend' proximally
- patient shakes his hand to obtain relief, classically at night

#### Examination

- weakness of thumb abduction (abductor pollicis brevis)
- wasting of thenar eminence (NOT hypothenar)
- Tinel's sign: tapping causes paraesthesia
- Phalen's sign: flexion of wrist causes symptoms

#### Causes

- idiopathic
- pregnancy
- oedema e.g. heart failure

- lunate fracture
- rheumatoid arthritis

## Electrophysiology

- motor + sensory: prolongation of the action potential

## Treatment

- corticosteroid injection
- wrist splints at night
- surgical decompression (flexor retinaculum division)

You are called to the obstetric ward to see a woman who is fitting. She is 34-weeks pregnant and currently an inpatient for the treatment of severe pre-eclampsia. The anaesthetist has secured the airway and is giving 100% oxygen. What is the most appropriate next step?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. IV calcium gluconate  |
| <input type="radio"/> | B. IV labetalol          |
| <input type="radio"/> | C. IV methyldopa         |
| <input type="radio"/> | D. IV lorazepam          |
| <input type="radio"/> | E. IV magnesium sulphate |

[Next question](#)

Eclampsia - give magnesium sulphate first-line

## Eclampsia

Eclampsia may be defined as the development of seizures in association pre-eclampsia. To recap, pre-eclampsia is defined as:

- condition seen after 20 weeks gestation
- pregnancy-induced hypertension
- proteinuria

Magnesium sulphate is used to both prevent seizures in patients with severe pre-eclampsia and treat seizures once they develop. Guidelines on its use suggest the following:

- should be given once a decision to deliver has been made
- in eclampsia an IV bolus of 4g over 5-10 minutes should be given followed by an infusion of 1g / hour
- urine output, reflexes, respiratory rate and oxygen saturations should be monitored during treatment
- treatment should continue for 24 hours after last seizure or delivery (around 40% of seizures occur post-partum)

Other important aspects of treating severe pre-eclampsia/eclampsia include fluid restriction to avoid the potentially serious consequences of fluid overload

A 56-year-old woman presents with facial asymmetry. Whilst brushing her teeth this morning she noted that the right hand corner of her mouth was drooping. She is generally well but noted some pain behind her right ear yesterday and says her right eye is becoming dry. On examination she has a complete paralysis of the facial nerve on the right side, extending from the forehead to the mouth. Ear, nose and throat examination is normal. Clinical examination of the peripheral nervous system is normal. What is the most likely diagnosis?

<input type="radio"/>	A. Ramsey-Hunt syndrome
<input type="radio"/>	B. Bell's palsy
<input type="radio"/>	C. Stroke
<input type="radio"/>	D. Multiple sclerosis
<input type="radio"/>	E. Parotid tumour

[Next question](#)

The pain around the ear raises the possibility of Ramsey-Hunt syndrome but this is actually quite common in Bell's palsy - some studies suggest it is seen in 50% of patients. The normal ear exam also goes against this diagnosis.

### Bell's palsy

Bell's palsy may be defined as an acute, unilateral, idiopathic, facial nerve paralysis. The aetiology is unknown although the role of the herpes simplex virus has been investigated previously.

#### Features

- lower motor neuron facial nerve palsy - forehead affected\*
- patients may also notice post-auricular pain (may precede paralysis), altered taste, dry eyes, hyperacusis

#### Management

- in the past a variety of treatment options have been proposed including no treatment, prednisolone only and a combination of aciclovir and prednisolone
- following a National Institute for Health randomised controlled trial it is now recommended that prednisolone 25mg bd for 10 days should be prescribed for patients within 72 hours of onset of Bell's palsy. Adding in aciclovir gives no additional benefit
- eye care is important - prescription of artificial tears and eye lubricants should be considered

#### Prognosis

- if untreated around 15% of patients have permanent moderate to severe weakness

\*upper motor neuron lesion 'spares' upper face

**Question 9 of 204**

Next

A 29-year-old woman with a past history of hypothyroidism presents to the surgery complaining of weakness, particularly of her arms, for the past four months. She has also developed double vision towards the end of the day, despite having a recent normal examination at the opticians. What is the most likely diagnosis?

<input type="radio"/>	A. Chronic fatigue syndrome
<input type="radio"/>	B. Polymyositis
<input type="radio"/>	C. Polymyalgia rheumatica
<input type="radio"/>	D. Multiple sclerosis
<input type="radio"/>	E. Myasthenia gravis

Next question

**Myasthenia gravis**

Myasthenia gravis is an autoimmune disorder resulting in insufficient functioning acetylcholine receptors. Antibodies to acetylcholine receptors are seen in 90% of cases\*. Myasthenia is more common in women (2:1)

The key feature is muscle fatigability - muscles become progressively weaker during periods of activity and slowly improve after periods of rest:

- extraocular muscle weakness: diplopia
- proximal muscle weakness: face, neck, limb girdle
- ptosis
- dysphagia

**Associations**

- thymomas in 15%
- autoimmune disorders: pernicious anaemia, autoimmune thyroid disorders, rheumatoid, SLE
- thymic hyperplasia in 50-70%

**Investigations**

- Tensilon test: IV edrophonium reduces muscle weakness temporarily
- CT thorax to exclude thymoma
- CK normal

**Management**

- long-acting anticholinesterase e.g. Pyridostigmine
- immunosuppression: prednisolone initially
- thymectomy

#### Management of myasthenic crisis

- plasmapheresis
- intravenous immunoglobulins

\*antibodies are less commonly seen in disease limited to the ocular muscles

Which one of the following statements regarding the development of a headache following lumbar puncture is incorrect?

<input type="radio"/>	A. Occurs in one-third of patients
<input type="radio"/>	B. May last several days
<input type="radio"/>	C. More common in females
<input type="radio"/>	D. Usually develops within the first 12 hours
<input type="radio"/>	E. Worsens with upright position

Next question

### Post-lumbar puncture headache

Headache following lumbar puncture (LP) occurs in approximately one-third of patients. The pathophysiology of is unclear but may relate to a 'leak' of CSF following dural puncture. Post-LP headaches are more common in young females with a low body mass index

#### Typical features

- usually develops within 24-48 hours following LP but may occur up to one week later
- may last several days
- worsens with upright position
- improves with recumbent position

Factors which may contribute to headache	Factors which do not contribute to headache
Increased needle size Direction of bevel Not replacing the stylet Increased number of LP attempts	Increased volume of CSF removed Bed rest following procedure Increased fluid intake post procedure Opening pressure of CSF Position of patient

#### Management

- supportive initially (analgesia, rest)
- if pain continues for more than 72 hours then specific treatment is indicated, to prevent subdural haematoma
- treatment options include: blood patch, epidural saline and intravenous caffeine

A 34-year-old female presents with vomiting preceded by an occipital headache of acute onset. On examination she was conscious and alert with photophobia but no neck stiffness. CT brain is reported as normal. What is the most appropriate further management?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. CT brain with contrast |
| <input type="radio"/> | B. Repeat CT brain in 24h |
| <input type="radio"/> | C. CSF examination        |
| <input type="radio"/> | D. Cerebral angiography   |
| <input type="radio"/> | E. MRI brain              |

Next question

If the CSF examination revealed xanthochromia, or there was still a high level of clinical suspicion, then cerebral angiography would be the next step.

### Subarachnoid haemorrhage

#### Causes

- 85% are due to rupture of berry aneurysms (conditions associated with berry aneurysms include adult polycystic kidney disease, Ehlers-Danlos syndrome and coarctation of the aorta)
- AV malformations
- trauma
- tumours

#### Investigations

- CT: negative in 5%
- LP: done after 12 hrs (allowing time for xanthochromia to develop)

#### Complications

- rebleeding (in 30%)
- obstructive hydrocephalus (due to blood in ventricles)
- vasospasm leading to cerebral ischaemia

#### Management

- neurosurgical opinion: no clear evidence over early surgical intervention against delayed intervention
- nimodipine (e.g. 60mg / 4 hrly, if BP allows) has been shown to reduce the severity of neurological deficits but doesn't reduce rebleeding\*

\*the way nimodipine works in subarachnoid haemorrhage is not fully understood. It has been previously postulated that it reduces cerebral vasospasm (hence maintaining cerebral perfusion) but this has not been demonstrated in studies



In patients with Guillain-Barre syndrome, respiratory function should be monitored with:

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Oxygen saturations    |
| <input type="radio"/> | B. PEFR                  |
| <input type="radio"/> | C. Flow volume loop      |
| <input type="radio"/> | D. Arterial blood gases  |
| <input type="radio"/> | E. Forced vital capacity |

Next question

FVC is used to monitor respiratory function in Guillain-Barre syndrome

### Guillain-Barre syndrome: management

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*).

#### Management

- plasma exchange
- IV immunoglobulins (IVIG): as effective as plasma exchange. No benefit in combining both treatments. IVIG may be easier to administer and tends to have fewer side-effects
- steroids and immunosuppressants have not been shown to be beneficial
- FVC regularly to monitor respiratory function

#### Prognosis

- 20% suffer permanent disability, 5% die

### Question 13 of 204

Next

A 73-year-old female with a history of recurrent falls at home and alcohol excess is brought to the Emergency Department due to episodes of confusion over the past 5 days. Between these episodes she is apparently her normal self. On examination her GCS is 14/15 and she has nystagmus on left lateral gaze. What is the most likely diagnosis?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. Subdural haemorrhage        |
| <input type="radio"/> | B. Subarachnoid haemorrhage    |
| <input type="radio"/> | C. Meningitis                  |
| <input type="radio"/> | D. Herpes simplex encephalitis |
| <input type="radio"/> | E. Alzheimer's disease         |

Next question

Fluctuating consciousness = subdural haemorrhage

The combination of falls, alcohol excess, fluctuating episodes of confusion and focal neurology points towards a diagnosis of subdural haemorrhage. The phrase 'fluctuating conscious level' is common in questions and should always bring to mind subdural haemorrhage

### Subdural haemorrhage

#### Basics

- most commonly secondary to trauma e.g. old person/alcohol falling over
- initial injury may be minor and is often forgotten
- caused by bleeding from damaged bridging veins between cortex and venous sinuses

#### Features

- headache
- classically fluctuating conscious level
- raised ICP

#### Treatment

- needs neurosurgical review ? burr hole

A 47-year-old man with a known history of schizophrenia is admitted to the Emergency Department due to confusion. A bottle of procyclidine tablets are found in his pocket. On examination the temperature is 38.1°C with a blood pressure of 155/100 mmHg. Neurological examination reveals a GCS of 13/15 but assessment of his peripheral nervous system is difficult due to generalised increased muscle tone. What is the most likely diagnosis?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Neuroleptic malignant syndrome    |
| <input type="radio"/> | B. Procyclidine overdose             |
| <input type="radio"/> | C. Catatonic schizophrenia           |
| <input type="radio"/> | D. Clozapine induced agranulocytosis |
| <input type="radio"/> | E. Quetiapine induced rhabdomyolysis |

[Next question](#)

### Neuroleptic malignant syndrome

Neuroleptic malignant syndrome is a rare but dangerous condition seen in patients taking antipsychotic medication. It carries a mortality of up to 10% and can also occur with atypical antipsychotics

#### Features

- more common in young male patients
- onset usually in first 10 days of treatment or after increasing dose
- pyrexia
- rigidity
- tachycardia

A raised creatine kinase is present in most cases. A leukocytosis may also be seen

#### Management

- stop antipsychotic
- IV fluids to prevent renal failure
- dantrolene may be useful in selected cases
- bromocriptine, dopamine agonist, may also be used

You review a 25-year-old man who is complaining of leg weakness. Other than a bout of diarrhoea three weeks ago he has been feeling fit and well and has no significant medical history. On examination you note reduced power in his legs, normal sensation and reduced knee and ankle reflexes. His pulse is 78/min and blood pressure is 122/84 mmHg (standing), 100/64 mmHg (sitting). What is the most likely diagnosis?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Botulism food poisoning |
| <input type="radio"/> | B. Guillain-Barre syndrome |
| <input type="radio"/> | C. Cauda equina syndrome   |
| <input type="radio"/> | D. Myasthenia gravis       |
| <input type="radio"/> | E. Transverse myelitis     |

[Next question](#)

### Guillain-Barre syndrome: features

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*).

The characteristic features of Guillain-Barre syndrome is progressive weakness of all four limbs. The weakness is classically ascending i.e. the lower extremities are affected first, however it tends to affect proximal muscles earlier than the distal ones. Sensory symptoms tend to be mild (e.g. distal paraesthesia) with very few sensory signs. Some patients experience back pain in the initial stages of the illness

#### Other features

- areflexia
- cranial nerve involvement e.g. diplopia
- autonomic involvement: e.g. urinary retention

#### Less common findings

- papilloedema: thought to be secondary to reduced CSF resorption

A 27-year-old man presents with a history of fits consistent with tonic-clonic seizures. What is the most suitable first-line treatment?

<input type="radio"/>	A. Gabapentin
<input type="radio"/>	B. Lamotrigine
<input type="radio"/>	C. Sodium valproate
<input type="radio"/>	D. Carbamazepine
<input type="radio"/>	E. Phenytoin

[Next question](#)

#### Epilepsy medication: first-line

- generalised seizure: sodium valproate
- partial seizure: carbamazepine

#### Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

#### Generalised tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

#### Absence seizures\* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

## Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

## Partial seizures

- carbamazepine
- second line: lamotrigine\*\*, sodium valproate

\*carbamazepine may actually exacerbate absence seizure

\*\*the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

Which of the following features is least likely to be found in a patient with tuberous sclerosis?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Adenoma sebaceum   |
| <input type="radio"/> | B. Cafe-au-lait spots |
| <input type="radio"/> | C. Retinal hamartomas |
| <input type="radio"/> | D. 'Ash-leaf' spots   |
| <input type="radio"/> | E. Lisch nodules      |

Next question

Lisch nodules are seen in neurofibromatosis

### Tuberous sclerosis

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous

#### Cutaneous features

- depigmented 'ash-leaf' spots which fluoresce under UV light
- roughened patches of skin over lumbar spine (Shagreen patches)
- adenoma sebaceum: butterfly distribution over nose
- fibromata beneath nails (subungual fibromata)
- café-au-lait spots\* may be seen

#### Neurological features

- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment

#### Also

- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- gliomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata

\*these of course are more commonly associated with neurofibromatosis. However a 1998 study of 106 children with TS found café-au-lait spots in 28% of patients

Which of the following visual field changes would be most consistent with a left parietal lobe lesion?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Right homonymous hemianopia              |
| <input type="radio"/> | B. Left inferior homonymous quadrantanopia  |
| <input type="radio"/> | C. Left superior homonymous quadrantanopia  |
| <input type="radio"/> | D. Right superior homonymous quadrantanopia |
| <input type="radio"/> | E. Right inferior homonymous quadrantanopia |

Next question

Visual field defects:

- left homonymous hemianopia means visual field defect to the left, i.e. lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

### Visual field defects

The main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

A congruous defect simply means complete or symmetrical visual field loss and conversely an incongruous defect is incomplete or asymmetric. Please see the link for an excellent diagram.

Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias\*

- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)



## Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

\*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details:

<http://www.ncbi.nlm.nih.gov/pubmed/9109741>

A 52-year-old man is prescribed apomorphine. What type of receptors does apomorphine act on?

- |                                  |                          |
|----------------------------------|--------------------------|
| <input type="radio"/>            | A. Opioid receptors      |
| <input type="radio"/>            | B. GABA receptors        |
| <input type="radio"/>            | C. Cholinergic receptors |
| <input checked="" type="radio"/> | D. Dopamine receptors    |
| <input type="radio"/>            | E. Muscarinic receptors  |

Next question

Apomorphine is one of the older dopamine receptor agonists. Newer agents such as ropinirole and cabergoline have since been developed

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline

- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

#### Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

#### COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

#### Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benztropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

An obese 24-year-old female presents with headaches and blurred vision. Examination reveals bilateral blurring of the optic discs but is otherwise unremarkable with no other neurological signs. Blood pressure is 130/74 and she is apyrexial. What is the most likely underlying diagnosis?

<input type="radio"/>	A. Multiple sclerosis
<input type="radio"/>	B. Meningococcal meningitis
<input type="radio"/>	C. Brain abscess
<input type="radio"/>	D. Normal pressure hydrocephalus
<input type="radio"/>	E. Idiopathic intracranial hypertension

[Next question](#)

Obese, young female with headaches / blurred vision think idiopathic intracranial hypertension

The combination of a young, obese female with papilloedema but otherwise normal neurology makes idiopathic intracranial hypertension the most likely diagnosis

### Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (also known as pseudotumour cerebri and formerly benign intracranial hypertension) is a condition classically seen in young, overweight females.

#### Features

- headache
- blurred vision
- papilloedema (usually present)
- enlarged blind spot
- sixth nerve palsy may be present

#### Risk factors

- obesity
- female sex
- pregnancy
- drugs\*: oral contraceptive pill, steroids, tetracycline, vitamin A

#### Management

- weight loss

- diuretics e.g. acetazolamide
- repeated lumbar puncture
- surgery: optic nerve sheath decompression and fenestration may be needed to prevent damage to the optic nerve. A lumboperitoneal or ventriculoperitoneal shunt may also be performed to reduce intracranial pressure

\*if intracranial hypertension is thought to occur secondary to a known causes (e.g. Medication) then it is of course not idiopathic

A 60-year-old woman presents with a tremor. Which one of the following features would suggest a diagnosis of essential tremor rather than Parkinson's disease?

<input type="radio"/>	A. Difficulty in initiating movement
<input type="radio"/>	B. Tremor is worse following alcohol
<input type="radio"/>	C. Postural instability
<input type="radio"/>	D. Unilateral symptoms
<input type="radio"/>	E. Tremor is worse when the arms are outstretched

Next question

Difficulty in initiating movement (bradykinesia), postural instability and unilateral symptoms (initially) are typical of Parkinson's. Essential tremor symptoms are usually eased by alcohol.

### Essential tremor

Essential tremor (previously called benign essential tremor) is an autosomal dominant condition which usually affects both upper limbs

#### Features

- postural tremor: worse if arms outstretched
- improved by alcohol and rest
- most common cause of titubation (head tremor)

#### Management

- propranolol is first-line
- primidone is sometimes used

A 24-year-old female presents with a headache. She has a past history of epilepsy and is known to suffer from migraines, but has previously managed attacks with a combination of paracetamol and metoclopramide. This combination is however not working for the current episode.

What second line medication is it most appropriate to use?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Codeine + paracetamol      |
| <input type="radio"/> | B. Pizotifen                  |
| <input type="radio"/> | C. Zolmitriptan + paracetamol |
| <input type="radio"/> | D. Methysergide               |
| <input type="radio"/> | E. Ergotamine                 |

Next question

Epilepsy is not a contraindication to the use of triptans. Opioids are not recommended in the management of migraine

### Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. NICE produced guidelines in 2012 on the management of headache, including migraines.

#### Acute treatment

- first-line: offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol
- for young people aged 12-17 years consider a nasal triptan in preference to an oral triptan
- if the above measures are not effective or not tolerated offer a non-oral preparation of metoclopramide\* or prochlorperazine and consider adding a non-oral NSAID or triptan

#### Prophylaxis

- prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients.
- NICE advise either topiramate or propranolol 'according to the person's preference, comorbidities and risk of adverse events'. Propranolol should be used in preference to topiramate in women of child bearing age as it may be teratogenic and it can reduce the effectiveness of hormonal contraceptives
- if these measures fail NICE recommend 'a course of up to 10 sessions of acupuncture over 5-8 weeks' or gabapentin
- NICE recommend: 'Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people'
- for women with predictable menstrual migraine treatment NICE recommend either frovatriptan (2.5 mg twice a day) or zolmitriptan (2.5 mg twice or three times a day) as a type of 'mini-prophylaxis'
- pizotifen is no longer recommend. Adverse effects such as weight gain & drowsiness are common

\*caution should be exercised with young patients as acute dystonic reactions may develop

**Question 23 of 204**

Next

A 45-year-old man presents with dizziness and right-sided hearing loss. Which one of the following tests would most likely indicate an acoustic neuroma?

<input type="radio"/>	A. Jerky nystagmus
<input type="radio"/>	B. Left homonymous hemianopia
<input type="radio"/>	C. Tongue deviated to the left
<input type="radio"/>	D. Fasciculation of the tongue
<input type="radio"/>	E. Absent corneal reflex

Next question

Loss of corneal reflex - think acoustic neuroma

**Acoustic neuroma**

Acoustic neuromas (more correctly called vestibular schwannomas) account for approximately five percent of intracranial tumours and 90 percent of cerebellopontine angle

Features can be predicted by the affected cranial nerves

- cranial nerve VIII: hearing loss, vertigo, tinnitus
- cranial nerve V: absent corneal reflex
- cranial nerve VII: facial palsy

Bilateral acoustic neuromas are seen in neurofibromatosis type 2

MRI of the cerebellopontine angle is the investigation of choice



A 57-year-old woman presents with an 8 week history of intermittent dizziness. These episodes typically occur when she suddenly moves her head and are characterised by the sensation that the room is 'spinning'. Most attacks last around one minute before dissipating. Neurological examination is unremarkable. What is the most likely diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Benign paroxysmal positional vertigo  |
| <input type="radio"/> | B. Meniere disease                       |
| <input type="radio"/> | C. Crescendo transient ischaemic attacks |
| <input type="radio"/> | D. Multiple sclerosis                    |
| <input type="radio"/> | E. Viral labyrinthitis                   |

[Next question](#)

Viral labyrinthitis typically causes constant symptoms of a shorter duration. Patients with Meniere disease usually have associated hearing loss and tinnitus. Also, the vertigo associated with Meniere disease typically lasts much longer.

### Benign paroxysmal positional vertigo

Benign paroxysmal positional vertigo (BPPV) is one of the most common causes of vertigo encountered. It is characterised by the sudden onset of dizziness and vertigo triggered by changes in head position

#### Features

- vertigo triggered by change in head position (e.g. rolling over in bed or gazing upwards)
- may be associated with nausea
- each episode typically lasts 10-20 seconds
- positive Halpike manoeuvre

BPPV has a good prognosis and usually resolves spontaneously after a few weeks to months. Symptomatic relief may be gained by:

- Epley manoeuvre (successful in around 80% of cases)
- teaching the patient exercises they can do themselves at home, for example Brandt-Daroff exercises

Medication is often prescribed (e.g. Betahistine) but it tends to be of limited value

Which one of the following is least associated with normal pressure hydrocephalus?

<input type="radio"/>	A. Papilloedema
<input type="radio"/>	B. Dementia
<input type="radio"/>	C. Urinary incontinence
<input type="radio"/>	D. Gait abnormality
<input type="radio"/>	E. Enlarged fourth ventricle

Next question

Urinary incontinence + gait abnormality + dementia = normal pressure hydrocephalus

### Normal pressure hydrocephalus

Normal pressure hydrocephalus is a reversible cause of dementia seen in elderly patients. It is thought to be secondary to reduced CSF absorption at the arachnoid villi. These changes may be secondary to head injury, subarachnoid haemorrhage or meningitis

A classical triad of features is seen

- urinary incontinence
- dementia and bradyphrenia
- gait abnormality (may be similar to Parkinson's disease)

Imaging

- hydrocephalus with an enlarged fourth ventricle

Management

- ventriculoperitoneal shunting

A 33-year-old man presents complaining of visual disturbance. Examination reveals a bitemporal hemianopia with predominately the upper quadrants being affected. What is the most likely lesion?

<input type="radio"/>	A. Craniopharyngioma
<input type="radio"/>	B. Brainstem lesion
<input type="radio"/>	C. Pituitary macroadenoma
<input type="radio"/>	D. Frontal lobe lesion
<input type="radio"/>	E. Right occipital lesion

[Next question](#)

### Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

An upper quadrant defect implies inferior chiasmal compression making a pituitary macroadenoma the most likely diagnosis

### Visual field defects

The main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

A congruous defect simply means complete or symmetrical visual field loss and conversely an incongruous defect is incomplete or asymmetric. Please see the link for an excellent diagram.

### Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

### Homonymous quadrantanopias\*

- superior: lesion of temporal lobe

- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

#### Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

\*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details:

<http://www.ncbi.nlm.nih.gov/pubmed/9109741>

A 28-year-old man develops nausea and a severe headache whilst trekking in Nepal. Within the next hour he becomes ataxic and confused. A diagnosis of high altitude cerebral oedema is suspected. Other than descent and oxygen, what is the most important treatment?

<input type="radio"/>	A. Acetazolamide
<input type="radio"/>	B. Dexamethasone
<input type="radio"/>	C. Burr hole
<input type="radio"/>	D. Mannitol
<input type="radio"/>	E. Frusemide

[Next question](#)

Acetazolamide is used more in the prevention of high altitude cerebral oedema.

### Altitude related disorders

There are three main types of altitude related disorders: acute mountain sickness (AMS), which may progress to high altitude pulmonary edema (HAPE) or high altitude cerebral edema (HACE). All three conditions are due to the chronic hypobaric hypoxia which develops at high altitudes

Acute mountain sickness is generally a self-limiting condition. Features of AMS start to occur above 2,500 - 3,000m, developing gradually over 6-12 hours and potentially last a number of days:

- headache
- nausea
- fatigue

#### Prevention and treatment of AMS

- the risk of AMS may actually be positively correlated to physical fitness
- gain altitude at no more than 500 m per day
- acetazolamide (a carbonic anhydrase inhibitor) is widely used to prevent AMS and has a supporting evidence base
- treatment: descent

A minority of people above 4,000m go onto develop high altitude pulmonary oedema (HAPE) or high altitude cerebral oedema (HACE), potentially fatal conditions

- HAPE presents with classical pulmonary oedema features
- HACE presents with headache, ataxia, papilloedema

## Management of HACE

- descent
- dexamethasone

## Management of HAPE

- descent
- nifedipine, dexamethasone, acetazolamide, phosphodiesterase type V inhibitors\*
- oxygen if available

\*the relative merits of these different treatments has only been studied in small trials. All seem to work by reducing systolic pulmonary artery pressure

A patient is referred due to the development of a third nerve palsy associated with a headache. On examination meningism is present. Which one of the following diagnoses needs to be urgently excluded?

- |                                  |  |
|----------------------------------|--|
| <input type="radio"/>            | A. Weber's syndrome                        |
| <input type="radio"/>            | B. Internal carotid artery aneurysm        |
| <input type="radio"/>            | C. Multiple sclerosis                      |
| <input checked="" type="radio"/> | D. Posterior communicating artery aneurysm |
| <input type="radio"/>            | E. Anterior communicating artery aneurysm  |

[Next question](#)

Painful third nerve palsy = posterior communicating artery aneurysm

Given the combination of a headache and third nerve palsy it is important to exclude a posterior communicating artery aneurysm

### Third nerve palsy

#### Features

- eye is deviated 'down and out'
- ptosis
- pupil may be dilated (sometimes called a 'surgical' third nerve palsy)

#### Causes

- diabetes mellitus
- vasculitis e.g. temporal arteritis, SLE
- false localizing sign\* due to uncal herniation through tentorium if raised ICP
- posterior communicating artery aneurysm (pupil dilated)
- cavernous sinus thrombosis
- Weber's syndrome: ipsilateral third nerve palsy with contralateral hemiplegia -caused by midbrain strokes
- other possible causes: amyloid, multiple sclerosis

\*this term is usually associated with sixth nerve palsies but it may be used for a variety of neurological presentations

Which one of the following features is most associated with frontal lobe lesions?

<input type="radio"/>	A. Wernicke's aphasia
<input type="radio"/>	B. Gerstmann's syndrome
<input type="radio"/>	C. Perseveration
<input type="radio"/>	D. Cortical blindness
<input type="radio"/>	E. Superior homonymous quadrantanopia

Next question

## Brain lesions

The following neurological disorders/features may allow localisation of a brain lesion:

### Gross anatomy

#### Parietal lobe lesions

- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

#### Occipital lobe lesions

- homonymous hemianopia (with macula sparing)
- cortical blindness
- visual agnosia

#### Temporal lobe lesion

- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia
- prosopagnosia (difficulty recognising faces)

#### Frontal lobes lesions



- expressive (Broca's) aphasia: located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus
- disinhibition
- perseveration
- anosmia
- inability to generate a list

## Cerebellum lesions

- midline lesions: gait and truncal ataxia
- hemisphere lesions: intention tremor, past pointing, dysdiadokinesis, nystagmus

## More specific areas

Medial thalamus and mammillary bodies of the hypothalamus	Wernicke and Korsakoff syndrome
Subthalamic nucleus of the basal ganglia	Hemiballism
Striatum (caudate nucleus) of the basal ganglia	Huntington chorea
Substantia nigra of the basal ganglia	Parkinson's disease
Amygdala	KluverBucy syndrome (hypersexuality, hyperorality, hyperphagia, visual agnosia)

A 21-year-old female is seen in the first seizure clinic in the outpatient department. Both the EEG and MRI brain are normal. A decision is made not to start her on anti-epileptic medication. What restrictions on driving should she be informed about?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. No restrictions but inform DVLA                              |
| <input type="radio"/> | B. No restrictions, no need to inform DVLA if not on medication |
| <input type="radio"/> | C. Cannot drive for 1 month from date of seizure                |
| <input type="radio"/> | D. Cannot drive for 6 months from date of seizure               |
| <input type="radio"/> | E. Cannot drive for 1 year from date of seizure                 |

Next question

Patients cannot drive for 6 months following a seizure

### DVLA: neurological disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

#### Specific rules

- first seizure: 6 months off driving\*. For patients with established epilepsy they must be fit free for 12 months before being able to drive
- stroke or TIA: 1 month off driving
- multiple TIAs over short period of times: 3 months off driving
- craniotomy e.g. For meningioma: 1 year off driving\*\*
- pituitary tumour: craniotomy: 6 months; trans-sphenoidal surgery 'can drive when there is no debarring residual impairment likely to affect safe driving'
- narcolepsy/cataplexy: cease driving on diagnosis, can restart once 'satisfactory control of symptoms'

#### Syncope

- simple faint: no restriction
- unexplained, low risk of recurrence: 4 weeks off
- explained and treated: 4 weeks off
- unexplained: 6 months off

\*previously rule was 12 months. It is now 6 months off driving if the licence holder has undergone assessment by

an appropriate specialist and no relevant abnormality has been identified on investigation, for example EEG and brain scan where indicated

\*\*if the tumour is a benign meningioma and there is no seizure history, licence can be reconsidered 6 months after surgery if remains seizure free

**Question 31 of 204**

Next

A 75-year-old female presents with weakness of her left hand. On examination wasting of the hypothenar eminence is seen and there is weakness of finger abduction. Thumb adduction is also weak. Where is the lesion most likely to be?

<input type="radio"/>	A. C7
<input type="radio"/>	B. Median nerve
<input type="radio"/>	C. Radial nerve
<input type="radio"/>	D. Anterior interosseous nerve
<input type="radio"/>	E. Ulnar nerve

Next question

**Ulnar nerve**

## Overview

- arises from medial cord of brachial plexus (C8, T1)

## Motor to

- medial two lumbricals
- adductor pollicis
- interossei
- hypothenar muscles: abductor digiti minimi, flexor digiti minimi
- flexor carpi ulnaris

## Sensory to

- medial 1 1/2 fingers (palmar and dorsal aspects)

**Patterns of damage**

## Damage at wrist

- 'claw hand' - hyperextension of the metacarpophalangeal joints and flexion at the distal and proximal interphalangeal joints of the 4th and 5th digits
- wasting and paralysis of intrinsic hand muscles (except lateral two lumbricals)
- wasting and paralysis of hypothenar muscles

- sensory loss to the medial 1 1/2 fingers (palmar and dorsal aspects)

#### Damage at elbow

- as above (however, ulnar paradox - clawing is more severe in distal lesions)
- radial deviation of wrist

Which type of motor neuron disease carries the worst prognosis?

<input type="radio"/>	A. Relapsing-remitting
<input type="radio"/>	B. Progressive bulbar palsy
<input type="radio"/>	C. Progressive muscular atrophy
<input type="radio"/>	D. Spinocerebellar ataxia
<input type="radio"/>	E. Amyotrophic lateral sclerosis

Next question

### Motor neuron disease: types

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, primary lateral sclerosis, progressive muscular atrophy and progressive bulbar palsy. In some patients however, there is a combination of clinical patterns

Amyotrophic lateral sclerosis (50% of patients)

- typically LMN signs in arms and UMN signs in legs
- in familial cases the gene responsible lies on chromosome 21 and codes for superoxide dismutase

Primary lateral sclerosis

- UMN signs only

Progressive muscular atrophy

- LMN signs only
- affects distal muscles before proximal
- carries best prognosis

Progressive bulbar palsy

- palsy of the tongue, muscles of chewing/swallowing and facial muscles due to loss of function of brainstem motor nuclei
- carries worst prognosis

A 65-year-old man is referred to the neurology outpatient clinic due to a resting tremor of his right hand. A diagnosis of Parkinson's disease is made. He is otherwise well and is not currently disabled by his symptoms. What is the most appropriate treatment?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Selegiline  |
| <input type="radio"/> | B. No treatment  |
| <input type="radio"/> | C. New generation dopamine receptor agonist e.g. ropinirole  |
| <input type="radio"/> | D. Conventional dopamine receptor agonist e.g. bromocriptine |
| <input type="radio"/> | E. Antimuscarinics   |

[Next question](#)

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

#### Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

#### COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

#### Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benzotropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction



Which one of the following features is most associated with temporal lobe lesions?

<input type="radio"/>	A. Astereognosis
<input type="radio"/>	B. Auditory agnosia
<input type="radio"/>	C. Visual agnosia
<input type="radio"/>	D. Disinhibition
<input type="radio"/>	E. Expressive (Broca's) aphasia

Next question

## Brain lesions

The following neurological disorders/features may allow localisation of a brain lesion:

### Gross anatomy

#### Parietal lobe lesions

- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

#### Occipital lobe lesions

- homonymous hemianopia (with macula sparing)
- cortical blindness
- visual agnosia

#### Temporal lobe lesion

- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia
- prosopagnosia (difficulty recognising faces)

#### Frontal lobes lesions

- expressive (Broca's) aphasia: located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus
- disinhibition
- perseveration
- anosmia
- inability to generate a list

## Cerebellum lesions

- midline lesions: gait and truncal ataxia
- hemisphere lesions: intention tremor, past pointing, dysdiadokinesis, nystagmus

## More specific areas

Medial thalamus and mammillary bodies of the hypothalamus	Wernicke and Korsakoff syndrome
Subthalamic nucleus of the basal ganglia	Hemiballism
Striatum (caudate nucleus) of the basal ganglia	Huntington chorea
Substantia nigra of the basal ganglia	Parkinson's disease
Amygdala	KluverBucy syndrome (hypersexuality, hyperorality, hyperphagia, visual agnosia)

Each of the following features are seen in myotonic dystrophy, except:

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Mild mental impairment |
| <input type="radio"/> | B. Round face             |
| <input type="radio"/> | C. Frontal balding        |
| <input type="radio"/> | D. Myotonia               |
| <input type="radio"/> | E. Cataracts              |

Next question

### Dystrophia myotonica - DM1

- distal weakness initially
- autosomal dominant
- diabetes
- dysarthria

## Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

### Genetics

- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	DM2
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent - Severe congenital form not seen

## General features

- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

## Other features

- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia

A 25-year-old female with a history of bilateral vitreous haemorrhage is referred due to progressive ataxia. What is the likely diagnosis?

<input type="radio"/>	A. Neurofibromatosis type I
<input type="radio"/>	B. Neurofibromatosis type II
<input type="radio"/>	C. Tuberose sclerosis
<input checked="" type="radio"/>	D. Von Hippel-Lindau syndrome
<input type="radio"/>	E. Sarcoidosis

[Next question](#)

Retinal and cerebellar haemangiomas are key features of Von Hippel-Lindau syndrome. Retinal haemangiomas are bilateral in 25% of patients and may lead to vitreous haemorrhage

### Von Hippel-Lindau syndrome

Von Hippel-Lindau (VHL) syndrome is an autosomal dominant condition predisposing to neoplasia. It is due to an abnormality in the VHL gene located on short arm of chromosome 3

#### Features

- cerebellar haemangiomas:
- retinal haemangiomas: vitreous haemorrhage
- renal cysts (premalignant)
- pheochromocytoma
- extra-renal cysts: epididymal, pancreatic, hepatic
- endolymphatic sac tumours

A 78-year-old man is seen in the Memory clinic. His daughter reports that for the past 12 months he has become increasingly forgetful and has now started to wander around at night. A mini-mental test is performed and he scores 18 out of 30. Neurological examination is unremarkable. A full blood screen is also requested, all of which comes back as normal. What is the most appropriate next step?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Arrange a MRI head   |
| <input type="radio"/> | B. Perform carotid Dopplers   |
| <input type="radio"/> | C. Give practical advice + advise family to contact Alzheimer's Society |
| <input type="radio"/> | D. Prescribe aspirin + simvastatin                                      |
| <input type="radio"/> | E. Prescribe donepezil  |

Next question

Neuroimaging is required to diagnose dementia

## Dementia

Dementia is thought to affect over 700,000 people in the UK and accounts for a large amount of health and social care spending. The most common cause of dementia in the UK is Alzheimer's disease followed by vascular and Lewy body dementia. These conditions may coexist.

### Features

- diagnosis can be difficult and is often delayed
- the mini-mental state examination is widely used. A score of 24 or less out of 30 suggests dementia

### Management

- in primary care a blood screen is usually sent to exclude reversible causes (e.g. Hypothyroidism). NICE recommend the following tests: FBC, U&E, LFTs, calcium, glucose, TFTs, vitamin B12 and folate levels. Patients are now commonly referred on to old-age psychiatrists (sometimes working in 'memory clinics').
- in secondary care neuroimaging is performed\* to exclude other reversible conditions (e.g. Subdural haematoma, normal pressure hydrocephalus) and help provide information on aetiology to guide prognosis and management

\*in the 2011 NICE guidelines structural imaging was said to be essential in the investigation of dementia

You want to prescribe an antiemetic to a 19-year-old female who is having a migraine attack. Which one of the following medications is most likely to precipitate extrapyramidal side-effects?

<input type="radio"/>	A. Meptazinol
<input type="radio"/>	B. Ondansetron
<input type="radio"/>	C. Domperidone
<input type="radio"/>	D. Cyclizine
<input type="radio"/>	E. Metoclopramide

[Next question](#)

Extrapyramidal side-effects are particularly common in children and young adults.

### Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. NICE produced guidelines in 2012 on the management of headache, including migraines.

#### Acute treatment

- first-line: offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol
- for young people aged 12-17 years consider a nasal triptan in preference to an oral triptan
- if the above measures are not effective or not tolerated offer a non-oral preparation of metoclopramide\* or prochlorperazine and consider adding a non-oral NSAID or triptan

#### Prophylaxis

- prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients.
- NICE advise either topiramate or propranolol 'according to the person's preference, comorbidities and risk of adverse events'. Propranolol should be used in preference to topiramate in women of child bearing age as it may be teratogenic and it can reduce the effectiveness of hormonal contraceptives
- if these measures fail NICE recommend 'a course of up to 10 sessions of acupuncture over 5-8 weeks' or gabapentin
- NICE recommend: 'Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people'
- for women with predictable menstrual migraine treatment NICE recommend either frovatriptan (2.5 mg twice a day) or zolmitriptan (2.5 mg twice or three times a day) as a type of 'mini-prophylaxis'
- pizotifen is no longer recommend. Adverse effects such as weight gain & drowsiness are common

\*caution should be exercised with young patients as acute dystonic reactions may develop

A 55-year-old man presents due to an uncontrollable urge to move his legs during the night-time. He has also experience the sensation of spiders crawling over his legs. Simple measures such as walking and massaging the affected limb have not alleviated the problem. What is the most appropriate medical therapy?

<input type="radio"/>	A. Selective serotonin reuptake inhibitor
<input type="radio"/>	B. Low-dose tricyclic antidepressant
<input type="radio"/>	C. Dopamine agonist
<input type="radio"/>	D. 5-HT3 antagonist
<input type="radio"/>	E. Dopamine antagonist

[Next question](#)

Restless leg syndrome - management includes dopamine agonists such as ropinirole

## Restless legs syndrome

Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. It is extremely common, affecting between 2-10% of the general population. Males and females are equally affected and a family history may be present

### Clinical features

- uncontrollable urge to move legs (akathisia). Symptoms initially occur at night but as condition progresses may occur during the day. Symptoms are worse at rest
- paraesthesias e.g. 'crawling' or 'throbbing' sensations
- movements during sleep may be noted by the partner - periodic limb movements of sleeps (PLMS)

### Causes and associations

- there is a positive family history in 50% of patients with idiopathic RLS
- iron deficiency anaemia
- uraemia
- diabetes mellitus
- pregnancy

The diagnosis is clinical although bloods to exclude iron deficiency anaemia may be appropriate

### Management



- simple measures: walking, stretching, massaging affected limbs
- treat any iron deficiency
- dopamine agonists are first-line treatment (e.g. Pramipexole, ropinirole)
- benzodiazepines
- gabapentin

A 34-year-old man is reviewed in the neurology clinic. He has been established on sodium valproate for primary generalised epilepsy. Despite now taking a therapeutic dose he continues to have seizures and is troubled by weight gain since starting sodium valproate. He asks to stop his current medication and try a different drug. Which one of the following drugs would be the most appropriate second-line treatment?

<input type="radio"/>	A. Lamotrigine
<input type="radio"/>	B. Ethosuximide
<input type="radio"/>	C. Pregabalin
<input type="radio"/>	D. Gabapentin
<input type="radio"/>	E. Tiagabine

[Next question](#)

Monotherapy with another drug should be attempted before combination therapy is started. Caution should be exercised when combining sodium valproate and lamotrigine as serious skin rashes such as Steven-Johnson's syndrome may be provoked

### Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Generalised tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures\* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

#### Partial seizures

- carbamazepine
- second line: lamotrigine\*\*, sodium valproate

\*carbamazepine may actually exacerbate absence seizure

\*\*the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

A 69-year-old man who is known to have Alzheimer's disease is reviewed in clinic. His latest Mini Mental State Examination

(MMSE) score is 18 out of 30. What is the most appropriate management?

<input type="radio"/>	A. Supportive care + memantine
<input type="radio"/>	B. Supportive care + trial of citalopram
<input type="radio"/>	C. Supportive care
<input type="radio"/>	D. Supportive care + donepezil + low-dose aspirin
<input type="radio"/>	E. Supportive care + donepezil

Next question

## Alzheimer's disease

Alzheimer's disease is a progressive degenerative disease of the brain accounting for the majority of dementia seen in the UK

### Genetics

- most cases are sporadic
- 5% of cases are inherited as an autosomal dominant trait
- mutations in the amyloid precursor protein (chromosome 21), presenilin 1 (chromosome 14) and presenilin 2 (chromosome 1) genes are thought to cause the inherited form
- apoprotein E allele E4 - encodes a cholesterol transport protein

### Pathological changes

- macroscopic = widespread cerebral atrophy, particularly involving the cortex and hippocampus
- microscopic = intraneuronal neurofibrillary tangles, neuronal plaques, deficiency of neurons
- biochemical = deposition of type A-Beta-amyloid protein in cortex, deficit of Ach from damage to an ascending forebrain projection

### Neurofibrillary tangles

- paired helical filaments are partly made from a protein called tau
- in AD are tau proteins are excessively phosphorylated

### Management

- NICE now recommend the three acetylcholinesterase inhibitors (donepezil, galantamine and rivastigmine) as options for managing mild to moderate Alzheimer's disease
- memantine is reserved for patients with moderate - severe Alzheimer's

A 76-year-old man is reviewed in the Elderly Medicine clinic. He is concerned about his increasing forgetfulness over the past six months. His daughter notes he has generally 'slowed down' and struggles to follow conversations. Over the past month he has noted increasingly frequent episodes of urinary incontinence. He has also had one episode of faecal incontinence in the past week. On examination he is noted to have brisk reflexes and a short, shuffling gait. No cerebellar signs are noted. What is the most likely diagnosis?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Multiple system atrophy       |
| <input type="radio"/> | B. Parkinson's disease           |
| <input type="radio"/> | C. Normal pressure hydrocephalus |
| <input type="radio"/> | D. Urinary tract infection       |
| <input type="radio"/> | E. Pick's disease                |

[Next question](#)

Urinary incontinence + gait abnormality + dementia = normal pressure hydrocephalus

The presence of dementia and absence of cerebellar signs point away from a diagnosis of multiple system atrophy

### Normal pressure hydrocephalus

Normal pressure hydrocephalus is a reversible cause of dementia seen in elderly patients. It is thought to be secondary to reduced CSF absorption at the arachnoid villi. These changes may be secondary to head injury, subarachnoid haemorrhage or meningitis

A classical triad of features is seen

- urinary incontinence
- dementia and bradyphrenia
- gait abnormality (may be similar to Parkinson's disease)

Imaging

- hydrocephalus with an enlarged fourth ventricle

Management

- ventriculoperitoneal shunting

A 55-year-old man is diagnosed with amyotrophic lateral sclerosis. Which one of the following drugs has been shown to confer a survival benefit?

<input type="radio"/>	A. Rituximab
<input type="radio"/>	B. Riluzole
<input type="radio"/>	C. Interferon-beta
<input type="radio"/>	D. Cyclophosphamide
<input type="radio"/>	E. Interferon-alpha

[Next question](#)

### Motor neuron disease: management

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy

#### Riluzole

- anti-glutamate drug
- used mainly in amyotrophic lateral sclerosis
- prolongs life by about 3 months
- expensive

#### Respiratory care

- non-invasive ventilation (usually BIPAP) is used at night
- studies have shown a survival benefit of around 7 months

#### Prognosis

- poor: 50% of patients die within 3 years

Which one of the following is least associated with the development of chorea?

<input type="radio"/>	A. Haemochromatosis
<input type="radio"/>	B. Ataxic telangiectasia
<input type="radio"/>	C. Carbon monoxide poisoning
<input type="radio"/>	D. SLE
<input type="radio"/>	E. Huntington's disease

Next question

## Chorea

Chorea describes involuntary, rapid, jerky movements which often move from one part of the body to another. Slower, sinuous movement of the limbs is termed athetosis. Chorea is caused by damage to the basal ganglia, especially the caudate nucleus.

### Causes of chorea

- Huntington's disease, Wilson's disease, ataxic telangiectasia
- SLE, anti-phospholipid syndrome
- rheumatic fever: Sydenham's chorea
- drugs: oral contraceptive pill, L-dopa, antipsychotics
- neuroacanthocytosis
- pregnancy: chorea gravidarum
- thyrotoxicosis
- polycythaemia rubra vera
- carbon monoxide poisoning
- cerebrovascular disease

**Question 45 of 204**

Next

A 33-year-old female with multiple sclerosis complains that her vision becomes blurred during a hot bath. What is this an example of?

<input type="radio"/>	A. Uhthoff's phenomenon
<input type="radio"/>	B. Oppenheim's sign
<input type="radio"/>	C. Werdnig-Hoffman's sign
<input type="radio"/>	D. Lambert's sign
<input type="radio"/>	E. Lhermitte's sign

Next question

This is Uhthoff's phenomenon. Lhermitte's sign describes paraesthesiae in the limbs on neck flexion

Oppenheim's sign is seen when scratching of the inner side of leg leads to extension of the toes. It is a sign of cerebral irritation and is not related to multiple sclerosis

Werdnig-Hoffman's disease is also known as spinal muscular atrophy

**Multiple sclerosis: features**

## Visual

- optic neuritis: common presenting feature
- optic atrophy
- Uhthoff's phenomenon: worsening of vision following rise in body temperature
- internuclear ophthalmoplegia

## Sensory

- pins/needles
- numbness
- trigeminal neuralgia
- Lhermitte's syndrome: paraesthesiae in limbs on neck flexion

## Motor

- spastic weakness

## Cerebellar

- ataxia



- tremor

## Others

- urinary incontinence
- sexual dysfunction
- intellectual deterioration

A 25-year-old female is found to have a left hemiparesis following a deep vein thrombosis. An ECG shows RBBB with right axis deviation. What is the most likely underlying diagnosis?

<input type="radio"/>	A. Ventricular septal defect
<input type="radio"/>	B. Patent ductus arteriosus
<input type="radio"/>	C. Ostium primum atrial septal defect
<input checked="" type="radio"/>	D. Ostium secundum atrial septal defect
<input type="radio"/>	E. Tetralogy of Fallot

[Next question](#)

The ostium secundum in this patient has allowed passage of an embolus from the right-sided circulation to the left causing a stroke

### Atrial septal defects

Atrial septal defects (ASDs) are the most likely congenital heart defect to be found in adulthood. They carry a significant mortality, with 50% of patients being dead at 50 years. Two types of ASDs are recognised, ostium secundum and ostium primum. Ostium secundum are the most common

#### Features

- ejection systolic murmur, fixed splitting of S2
- embolism may pass from venous system to left side of heart causing a stroke

#### Ostium secundum (70% of ASDs)

- associated with Holt-Oram syndrome (tri-phalangeal thumbs)
- ECG: RBBB with RAD

#### Ostium primum

- present earlier than ostium secundum defects
- associated with abnormal AV valves
- ECG: RBBB with LAD, prolonged PR interval

You are reviewing a 22-year-old man who has developed headaches. Which one of the following features is most typical of migraines?

<input type="radio"/>	A. Pain on neck flexion
<input type="radio"/>	B. Phonophobia
<input type="radio"/>	C. Epiphora
<input type="radio"/>	D. Recent viral illness
<input type="radio"/>	E. Bilateral, 'tight-band' like pain

[Next question](#)

Phonophobia occurs in around three-quarters of patients.

### Migraine: diagnostic criteria

The International Headache Society has produced the following diagnostic criteria for migraine without aura:

<b>A</b>	At least 5 attacks fulfilling criteria B-D
<b>B</b>	Headache attacks lasting 4-72 hours* (untreated or unsuccessfully treated)
<b>C</b>	Headache has at least two of the following characteristics: <ul style="list-style-type: none"> <li>1. unilateral location*</li> <li>2. pulsating quality (i.e., varying with the heartbeat)</li> <li>3. moderate or severe pain intensity</li> <li>4. aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)</li> </ul>
<b>D</b>	During headache at least one of the following: <ul style="list-style-type: none"> <li>1. nausea and/or vomiting*</li> <li>2. photophobia and phonophobia</li> </ul>
<b>E</b>	Not attributed to another disorder (history and examination do not suggest a secondary headache disorder or, if they do, it is ruled out by appropriate investigations or headache attacks do not occur for the first time in close temporal relation to the other disorder)

\*In children, attacks may be shorter-lasting, headache is more commonly bilateral, and gastrointestinal disturbance is more prominent.

Migraine with aura (around 1 in 3 migraine patients) tends to be easier to diagnose with a typical aura being progressive in nature and may occur hours prior to the headache. Typical aura include a transient hemianopic disturbance or a spreading scintillating scotoma ('jagged crescent'). Sensory symptoms may also occur

Which one of the following features is not associated with an oculomotor nerve palsy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Miosis   |
| <input type="radio"/> | B. Ptosis   |
| <input type="radio"/> | C. Eye is deviated 'down and out'                           |
| <input type="radio"/> | D. Pain if due to a posterior communicating artery aneurysm |
| <input type="radio"/> | E. Diplopia   |

Next question

Ptosis + dilated pupil = third nerve palsy; ptosis + constricted pupil = Horner's

Oculomotor nerve palsy is typically associated with a dilated pupil

### Third nerve palsy

#### Features

- eye is deviated 'down and out'
- ptosis
- pupil may be dilated (sometimes called a 'surgical' third nerve palsy)

#### Causes

- diabetes mellitus
- vasculitis e.g. temporal arteritis, SLE
- false localizing sign\* due to uncal herniation through tentorium if raised ICP
- posterior communicating artery aneurysm (pupil dilated)
- cavernous sinus thrombosis
- Weber's syndrome: ipsilateral third nerve palsy with contralateral hemiplegia -caused by midbrain strokes
- other possible causes: amyloid, multiple sclerosis

\*this term is usually associated with sixth nerve palsies but it may be used for a variety of neurological presentations

A 12-year-old boy is brought to the Emergency Department. He was hit on the side the head by a cricket ball during a match. His teacher describes him initially collapsing to the ground and complaining of a sore head. After two minutes he got up, said he felt OK and continued playing. After 30 minutes he suddenly collapsed to the ground and lost consciousness. What type of injury is he most likely to have sustained?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Cerebral contusion           |
| <input type="radio"/> | B. Subarachnoid haemorrhage     |
| <input type="radio"/> | C. Intraventricular haemorrhage |
| <input type="radio"/> | D. Extradural haematoma         |
| <input type="radio"/> | E. Subdural haematoma           |

[Next question](#)

Epidural haematoma - lucid interval

## Head injury

Types of traumatic brain injury:

<b>Extradural (epidural) haematoma</b>	<p>Bleeding into the space between the dura mater and the skull. Often results from acceleration-deceleration trauma or a blow to the side of the head. The majority of epidural haematomas occur in the temporal region where skull fractures cause a rupture of the middle meningeal artery.</p> <p>Features</p> <ul style="list-style-type: none"> <li>• features of raised intracranial pressure</li> <li>• some patients may exhibit a lucid interval</li> </ul>
<b>Subdural haematoma</b>	<p>Bleeding into the outermost meningeal layer. Most commonly occur around the frontal and parietal lobes.</p> <p>Risk factors include old age, alcoholism and anticoagulation.</p> <p>Slower onset of symptoms than a epidural haematoma.</p>
<b>Subarachnoid haemorrhage</b>	<p>Usually occurs spontaneously in the context of a ruptured cerebral aneurysm but may be seen in association with other injuries when a patient has sustained a traumatic brain injury</p>

A 45-year-old man presents to the Emergency Department following the sudden onset of pain in the right side of his face whilst hammering a nail into the wall. The pain is described as severe and constant. On examination he has a mild right ptosis and small right pupil. What is the most likely diagnosis?

<input type="radio"/>	A. Trigeminal neuralgia
<input type="radio"/>	B. Glaucoma
<input type="radio"/>	C. Carotid artery dissection
<input type="radio"/>	D. Syringomyelia
<input type="radio"/>	E. Migraine

Next question

This patient has Horner's syndrome caused by a carotid artery dissection. This may be caused by relatively benign trauma to the neck such as hyperextension whilst doing DIY. Cluster headache would be a differential diagnosis

### Horner's syndrome

#### Features

- miosis (small pupil)
- ptosis
- enophthalmos\* (sunken eye)
- anhydrosis (loss of sweating one side)

#### Distinguishing between causes

- heterochromia (difference in iris colour) is seen in congenital Horner's
- anhydrosis: see below

Central lesions	Pre-ganglionic lesions	Post-ganglionic lesions
Anhydrosis of the face, arm and trunk	Anhydrosis of the face	No anhydrosis
Stroke Syringomyelia Multiple sclerosis Tumour Encephalitis	Pancoast's tumour Thyroidectomy Trauma Cervical rib	Carotid artery dissection Carotid aneurysm Cavernous sinus thrombosis Cluster headache

\*in reality the appearance is due to a narrow palpebral aperture rather than true enophthalmos

Neurofibromatosis type 1 is associated with a gene defect on which chromosome?

- ☐ A. Chromosome 4
- ☐ B. Chromosome 11
- ☐ C. Chromosome 16
- ☒ D. Chromosome 17
- ☐ E. Chromosome 22

Next question

One of our registered users sent the following mnemonic to us:

- NF1: chromosome 17 - as neurofibromatosis has 17 characters
- NF2: chromosome 22 - all the 2's

### Neurofibromatosis

There are two types of neurofibromatosis, NF1 and NF2. Both are inherited in an autosomal dominant fashion

NF1 is also known as von Recklinghausen's syndrome. It is caused by a gene mutation on chromosome 17 which encodes neurofibromin and affects around 1 in 4,000

NF2 is caused by gene mutation on chromosome 22 and affects around 1 in 100,000

### Features

NF1	NF2
Café-au-lait spots ( $\geq 6$ , 15 mm in diameter) Axillary/groin freckles Peripheral neurofibromas Iris: Lisch nodules in $> 90\%$ Scoliosis	Bilateral acoustic neuromas

A 41-year-old man presents with a two week history of headaches around the left side of his face associated with watery eyes. He describes having about two episodes a day each lasting around 30 minutes. On examination he has a red left eye and a partial left ptosis. There is no past medical history of note other than migraines as a child. What is the likely diagnosis?

- |                                  |                                 |
|----------------------------------|---------------------------------|
| <input type="radio"/>            | A. Atypical migraine            |
| <input checked="" type="radio"/> | B. Cluster headache             |
| <input type="radio"/>            | C. Trigeminal neuralgia         |
| <input type="radio"/>            | D. Acute angle closure glaucoma |
| <input type="radio"/>            | E. Cavernous sinus thrombosis   |

Next question

Episodic eye pain, lacrimation, nasal stuffiness occurring daily - cluster headache

### Cluster headache

Cluster headaches\* are more common in men (5:1) and smokers

#### Features

- pain typical occurs once or twice a day, each episode lasting 15 mins - 2 hours
- clusters typically last 4-12 weeks
- intense pain around one eye (recurrent attacks 'always' affect same side)
- patient is restless during an attack
- accompanied by redness, lacrimation, lid swelling
- nasal stuffiness
- miosis and ptosis in a minority

#### Management

- acute: 100% oxygen, subcutaneous sumatriptan, nasal lidocaine
- prophylaxis: verapamil, prednisolone
- consider specialist referral

\*some neurologists use the term trigeminal autonomic cephalgia to group a number of conditions including cluster headache, paroxysmal hemicrania and short-lived unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). It is recommended such patients are referred for specialist assessment as specific treatment may be required, for example it is known paroxysmal hemicrania responds very well to indomethacin



A 55-year-old man is referred to the neurology clinic due to a resting tremor and an abnormal gait characterised by short, shuffling steps. Which one of the following features would point towards a diagnosis of Parkinson's disease rather than parkinsonism of another cause?

<input type="radio"/>	A. Asymmetrical tremor
<input type="radio"/>	B. Bradykinesia
<input type="radio"/>	C. Impairment of vertical gaze
<input type="radio"/>	D. Confusion
<input type="radio"/>	E. Poor response to levodopa therapy

[Next question](#)

Asymmetrical symptoms suggests idiopathic Parkinson's

### Parkinson's disease: features

Parkinson's disease is a progressive neurodegenerative condition caused by degeneration of dopaminergic neurons in the substantia nigra.. This results in a classic triad of features: bradykinesia, tremor and rigidity. The symptoms of Parkinson's disease are characteristically asymmetrical

#### Bradykinesia

- poverty of movement also seen: mask-like facies
- difficulty in initiating movement

#### Tremor

- most marked at rest, 3-5 Hz
- typically 'pill-rolling'

#### Rigidity

- lead pipe
- cogwheel: due to superimposed tremor

#### Other characteristic features

- flexed posture

- short, shuffling steps
- micrographia
- drooling of saliva
- psychiatric features: depression is the most common feature (affects about 40%); dementia, psychosis and sleep disturbances may also occur
- impaired olfaction
- REM sleep behaviour disorder

**Drug-induced parkinsonism** has slightly different features to Parkinson's disease:

- motor symptoms are generally rapid onset and bilateral
- rigidity and rest tremor are uncommon

A 40-year-old woman presents with recurrent episode of vertigo associated with a feeling or 'fullness' and 'pressure' in her ears. She thinks her hearing is worse during the attacks. Clinical examination is unremarkable. What is the most likely diagnosis?

<input type="radio"/>	A. Meniere's disease
<input type="radio"/>	B. Benign paroxysmal positional vertigo
<input type="radio"/>	C. Acoustic neuroma
<input type="radio"/>	D. Cholesteatoma
<input type="radio"/>	E. Somatisation

[Next question](#)

### Meniere's disease

Meniere's disease is a disorder of the inner ear of unknown cause. It is characterised by excessive pressure and progressive dilation of the endolymphatic system. It is more common in middle-aged adults but may be seen at any age. Meniere's disease has a similar prevalence in both men and women.

#### Features

- recurrent episodes of vertigo, tinnitus and hearing loss (sensorineural). Vertigo is usually the prominent symptom
- a sensation of aural fullness or pressure is now recognised as being common
- other features include nystagmus and a positive Romberg test
- episodes last minutes to hours
- typically symptoms are unilateral but bilateral symptoms may develop after a number of years

#### Natural history

- symptoms resolve in the majority of patients after 5-10 years
- some patients may be left with hearing loss
- psychological distress is common

#### Management

- ENT assessment is required to confirm the diagnosis
- patients should inform the DVLA. The current advice is to cease driving until satisfactory control of symptoms is achieved
- acute attacks: buccal or intramuscular prochlorperazine. Admission is sometimes required
- prevention: betahistine may be of benefit

A 64-year-old man presents with a eight-month history of generalised weakness. On examination he has fasciculation and weakness in both arms with absent reflexes. Examination of the lower limbs reveal increased tone and exaggerated reflexes. Sensation was normal and there were no cerebellar signs. What is the most likely diagnosis?

- ☐ A. Progressive muscular atrophy
- ☐ B. Amyotrophic lateral sclerosis
- ☐ C. Vitamin B12 deficiency
- ☐ D. Syringomyelia
- ☐ E. Multiple sclerosis

[Next question](#)

'Fasciculations' - think motor neuron disease

These symptoms are typical of amyotrophic lateral sclerosis, the most common type of motor neuron disease.

### Motor neuron disease: features

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy

There are a number of clues which point towards a diagnosis of motor neuron disease:

- fasciculation
- absence of sensory signs/symptoms\*
- lower motor neuron signs in arms and upper motor neuron signs in legs
- wasting of the small hand muscles/tibialis anterior is common

Other features

- doesn't affect external ocular muscles
- no cerebellar signs
- abdominal reflexes are usually preserved and sphincter dysfunction if present is a late feature

The diagnosis of motor neuron disease is clinical, but nerve conduction studies will show normal motor conduction and can help exclude a neuropathy. Electromyography shows a reduced number of action potentials with an increased amplitude. MRI is usually performed to exclude the differential diagnosis of cervical cord compression and myelopathy

\*vague sensory symptoms may occur early in the disease (e.g. limb pain) but 'never' sensory signs

A 64-year-old female is reviewed in the rapid access transient ischaemic attack clinic. For the past three weeks she has been having episodes of transient loss of vision in the right eye. Carotid ultrasound reveals a 48% stenosis of her right carotid artery and an ECG shows sinus rhythm. What is the most appropriate management of this patient?

- ☐ A. Warfarin
- ☐ B. Clopidogrel
- ☐ C. Carotid endarterectomy
- ☐ D. Aspirin
- ☐ E. Aspirin and dipyridamole

[Next question](#)

#### Antiplatelets

- TIA: aspirin & dipyridamole
- ischaemic stroke: clopidogrel

Carotid artery endarterectomy is recommend if the patient has suffered a stroke or TIA in the carotid territory and is not severely disabled. It should only be considered if the carotid stenosis is greater than 70% or 50%, depending on the reporting criteria used - please see below.

#### Transient ischaemic attack

NICE issued updated guidelines relating to stroke and transient ischaemic attack (TIA) in 2008. They advocated the use of the ABCD2 prognostic score for risk stratifying patients who've had a suspected TIA:

	Criteria	Points
<b>A</b>	Age $\geq$ 60 years	1
<b>B</b>	Blood pressure $\geq$ 140/90 mmHg	1
<b>C</b>	Clinical features	
	- Unilateral weakness	2
	- Speech disturbance, no weakness	1
<b>D</b>	Duration of symptoms	
	- > 60 minutes	2
	- 10-59 minutes	1
	Patient has diabetes	1

This gives a total score ranging from 0 to 7. People who have had a suspected TIA who are at a higher risk of stroke (that is, with an ABCD2 score of 4 or above) should have:

- aspirin (300 mg daily) started immediately
- specialist assessment and investigation within 24 hours of onset of symptoms
- measures for secondary prevention introduced as soon as the diagnosis is confirmed, including discussion of individual risk factors

If the ABCD2 risk score is 3 or below:

- specialist assessment within 1 week of symptom onset, including decision

on brain imaging

- if vascular territory or pathology is uncertain, refer for brain imaging

People with crescendo TIAs (two or more episodes in a week) should be treated as being at high risk of stroke, even though they may have an ABCD2 score of 3 or below.

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- aspirin plus modified-release (MR) dipyridamole is still recommended as first choice for people who have had a TIA, but now there is no recommended limit on the duration of treatment. Clopidogrel is not recommended
- MR dipyridamole monotherapy is recommended after TIA only if aspirin is contraindicated or not tolerated, again with no limit on duration of treatment.

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST\* criteria or > 50% according to NASCET\*\* criteria

\*European Carotid Surgery Trialists' Collaborative Group

\*\*North American Symptomatic Carotid Endarterectomy Trial

Which one of the following drugs is used in the management of multiple sclerosis?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Beta-interferon  |
| <input type="radio"/> | B. Gamma-interferon |
| <input type="radio"/> | C. Infliximab       |
| <input type="radio"/> | D. Rituximab        |
| <input type="radio"/> | E. Alpha-interferon |

Next question

### Multiple sclerosis: management

Treatment in multiple sclerosis is focused at reducing the frequency and duration of relapses. There is no cure. High dose steroids (e.g. IV methylprednisolone) may be given for 3-5 days to shorten the length of an acute relapse. Baclofen is helpful in controlling spasticity. Hallucinations are occasionally seen on the withdrawal of baclofen

Beta-interferon has been shown to reduce the relapse rate by up to 30%. Certain criteria have to be met before it is used:

- relapsing-remitting disease + 2 relapses in past 2 years + able to walk 100m unaided
- secondary progressive disease + 2 relapses in past 2 years + able to walk 10m (aided or unaided)
- reduces number of relapses and MRI changes, however doesn't reduce overall disability

Other drugs used in the management of multiple sclerosis include:

- glatiramer acetate: immunomodulating drug
- natalizumab: a recombinant monoclonal antibody that antagonises Alpha4Beta1-integrin found on the surface of leucocytes, thus inhibiting migration of leucocytes across the endothelium into parenchymal tissue

### Symptom control

- spasticity: baclofen and gabapentin are first-line. Other options include diazepam, dantrolene and tizanidine

**Question 58 of 204**

Next

A 34-year-old man from West Africa is admitted due to confusion associated with left-sided weakness and ataxia. He is known to be HIV positive but is not on anti-retroviral treatment. The following results are obtained:

CD4	43 u/l
CT head	Low attenuation diffusely. No mass effect or enhancement

What is the most likely diagnosis?

- ☐ A. Toxoplasmosis
- ☐ B. Tuberculosis
- ☐ C. Progressive multifocal leukoencephalopathy
- ☐ D. *Cryptococcus*
- ☐ E. Cerebral lymphoma

Next question

**HIV: neurocomplications****Generalised neurological disease****Encephalitis**

- may be due to CMV or HIV itself
- HSV encephalitis but is relatively rare in the context of HIV
- CT: oedematous brain

***Cryptococcus***

- most common fungal infection of CNS
- headache, fever, malaise, nausea/vomiting, seizures, focal neurological deficit
- CSF: high opening pressure, India ink test positive
- CT: meningeal enhancement, cerebral oedema
- meningitis is typical presentation but may occasionally cause a space occupying lesion

**Progressive multifocal leukoencephalopathy (PML)**

- widespread demyelination
- due to infection of oligodendrocytes by human papovirus (JC virus)
- symptoms, subacute onset : behavioural changes, speech, motor, visual impairment



- CT: single or multiple lesions, no mass effect, don't usually enhance. MRI is better - high-signal demyelinating white matter lesions are seen

#### AIDS dementia complex

- caused by HIV virus itself
- symptoms: behavioural changes, motor impairment
- CT: cortical and subcortical atrophy

### Focal neurological lesions

#### Toxoplasmosis

- accounts for around 50% of cerebral lesions in patients with HIV
- constitutional symptoms, headache, confusion, drowsiness
- CT: usually single or multiple ring enhancing lesions, mass effect may be seen
- management: sulfadiazine and pyrimethamine

#### Primary CNS lymphoma

- accounts for around 30% of cerebral lesions
- associated with the Epstein-Barr virus
- CT: single or multiple ring enhancing lesions

Differentiating between toxoplasmosis and lymphoma is a common clinical scenario in HIV patients. It is clearly important given the vastly different treatment strategies. The table below gives some general differences. Please see the Radiopaedia link for more details.

Toxoplasmosis	Lymphoma
Multiple lesions	Single lesion
Rng or nodular enhancement	Solid enhancement
Thallium SPECT negative	Thallium SPECT positive

#### Tuberculosis

- much less common than toxoplasmosis or primary CNS lymphoma
- CT: single enhancing lesion

Which one of the following is least characteristic of Wernicke's encephalopathy?

- |                       |                    |
|-----------------------|--------------------|
| <input type="radio"/> | A. Ataxia          |
| <input type="radio"/> | B. Confusion       |
| <input type="radio"/> | C. Ophthalmoplegia |
| <input type="radio"/> | D. Confabulation   |
| <input type="radio"/> | E. Nystagmus       |

Next question

An inability to acquire new memories and confabulation suggests the development of Korsakoff's syndrome

### Wernicke's encephalopathy

Wernicke's encephalopathy is a neuropsychiatric disorder caused by thiamine deficiency which is most commonly seen in alcoholics. Rarer causes include: persistent vomiting, stomach cancer, dietary deficiency. A classic triad of nystagmus, ophthalmoplegia and ataxia may occur. In Wernicke's encephalopathy petechial haemorrhages occur in a variety of structures in the brain including the mamillary bodies and ventricle walls

#### Features

- nystagmus (the most common ocular sign)
- ophthalmoplegia
- ataxia
- confusion, altered GCS
- peripheral sensory neuropathy

#### Investigations

- decreased red cell transketolase
- MRI

Treatment is with urgent replacement of thiamine

A 19-year-old female presents complaining of visual disturbance. Examination reveals a bitemporal hemianopia with predominately the lower quadrants being affected. What is the most likely lesion?

<input type="radio"/>	A. Brainstem lesion
<input type="radio"/>	B. Craniopharyngioma
<input type="radio"/>	C. Frontal lobe lesion
<input type="radio"/>	D. Pituitary macroadenoma
<input type="radio"/>	E. Right occipital lesion

[Next question](#)

### Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

### Visual field defects

The main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

A congruous defect simply means complete or symmetrical visual field loss and conversely an incongruous defect is incomplete or asymmetric. Please see the link for an excellent diagram.

### Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

### Homonymous quadrantanopias\*

- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe

- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

#### Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

\*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details:

<http://www.ncbi.nlm.nih.gov/pubmed/9109741>

An 80-year-old man is investigated for progressive cognitive impairment. Which one of the following features is most suggestive of Lewy body dementia?

<input type="radio"/>	A. Disinhibition
<input type="radio"/>	B. Emotional lability
<input type="radio"/>	C. Symptoms worsen with neuroleptics
<input type="radio"/>	D. Urinary incontinence
<input type="radio"/>	E. Paucity of extrapyramidal signs

[Next question](#)

### Lewy body dementia

Lewy body dementia is an increasingly recognised cause of dementia, accounting for up to 20% of cases. The characteristic pathological feature is alpha-synuclein cytoplasmic inclusions (Lewy bodies) in the substantia nigra, paralimbic and neocortical areas

The relationship between Parkinson's disease and Lewy body dementia is complicated, particularly as dementia is often seen in Parkinson's disease. Also, up to 40% of patients with Alzheimer's have Lewy bodies

Neuroleptics should be avoided in Lewy body dementia as patients are extremely sensitive and may develop irreversible parkinsonism. Questions may give a history of a patient who has deteriorated following the introduction of an antipsychotic agent

#### Features

- progressive cognitive impairment
- parkinsonism
- visual hallucinations (other features such as delusions and non-visual hallucinations may also be seen)

A 54-year-old man with small cell lung cancer complains of muscle weakness. Each one of the following are features of Lambert-Eaton syndrome, except:

<input type="radio"/>	A. Proximal muscles more commonly affected
<input type="radio"/>	B. Hyporeflexia
<input type="radio"/>	C. Dry mouth
<input type="radio"/>	D. Repeated muscle contractions lead to decreased muscle strength
<input type="radio"/>	E. Impotence

Next question

In myasthenia gravis repeated muscle contractions lead to reduced muscle strength. The opposite is however classically seen in the related disorder Lambert-Eaton syndrome

### Lambert-Eaton syndrome

Lambert-Eaton myasthenic syndrome is seen in association with small cell lung cancer, and to a lesser extent breast and ovarian cancer. It may also occur independently as an autoimmune disorder. Lambert-Eaton myasthenic syndrome is caused by an antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system

#### Features

- repeated muscle contractions lead to increased muscle strength\* (in contrast to myasthenia gravis)
- limb girdle weakness (affects lower limbs first)
- hyporeflexia
- autonomic symptoms: dry mouth, impotence, difficulty micturating
- ophthalmoplegia and ptosis not commonly a feature (unlike in myasthenia gravis)

#### EMG

- incremental response to repetitive electrical stimulation

#### Management

- treatment of underlying cancer
- immunosuppression, for example with prednisolone and/or azathioprine
- 3,4-diaminopyridine is currently being trialled\*\*
- intravenous immunoglobulin therapy and plasma exchange may be beneficial

\*in reality this is seen in only 50% of patients and following prolonged muscle use muscle strength will eventually

decrease

\*\*works by blocking potassium channel efflux in the nerve terminal so that the action potential duration is increased. Calcium channels can then be open for a longer time and allow greater acetylcholine release to the stimulate muscle at the end plate

A 54-year-old man is admitted to the Emergency Department with a left hemiplegia. His symptoms started around 5 hours ago and he has had no headache, visual disturbance or loss of consciousness. On examination a dense left hemiplegia is noted. Blood pressure is 120/78 mmHg, GCS is 15/15 and pupils are equal and reactive to light. An urgent CT scan is performed shortly after his arrival. This demonstrates no abnormality. What is the most appropriate initial management?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Enoxaparin    |
| <input type="radio"/> | B. Alteplase     |
| <input type="radio"/> | C. Dexamethasone |
| <input type="radio"/> | D. Warfarin      |
| <input type="radio"/> | E. Aspirin       |

[Next question](#)

Stroke thrombolysis - only consider if less than 3 hours and haemorrhage excluded

This patient has had an ischaemic stroke. He is however outside the thrombolytic window and should therefore be treated with aspirin

### Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued stroke guidelines in 2008, although they modified their guidance with respect to antiplatelet therapy in 2010.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy\*
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commenced on a statin. Many physicians will delay treatment until after at least 48 hours due to the risk of haemorrhagic transformation

### Thrombolysis

Thrombolysis should only be given if:



- it is administered within 3 hours\*\* of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

## Secondary prevention

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- clopidogrel is now recommended by NICE ahead of combination use of aspirin plus modified release (MR) dipyridamole in people who have had an ischaemic stroke
- aspirin plus MR dipyridamole is now recommended after an ischaemic stroke only if clopidogrel is contraindicated or not tolerated, but treatment is no longer limited to 2 years' duration
- MR dipyridamole alone is recommended after an ischaemic stroke only if aspirin or clopidogrel are contraindicated or not tolerated, again with no limit on duration of treatment

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST\*\*\* criteria or > 50% according to NASCET\*\*\*\* criteria

\*the 2009 Controlling hypertension and hypotension immediately post-stroke (CHHIPS) trial may change thinking on this but guidelines have yet to change to reflect this

\*\*SIGN recommend a window of 4.5 hours

\*\*\*European Carotid Surgery Trialists' Collaborative Group

\*\*\*\*North American Symptomatic Carotid Endarterectomy Trial

A 54-year-old man presents concerned about leg weakness. On examination he is noted to have increased tone in both legs, brisk reflexes and weakness in both lower limbs. Examination of his upper limbs is normal. Which one of the following is least likely to produce these symptoms?

<input type="radio"/>	A. HIV
<input type="radio"/>	B. Amyloidosis
<input type="radio"/>	C. Hereditary spastic paraplegia
<input type="radio"/>	D. Multiple sclerosis
<input type="radio"/>	E. Parasagittal meningioma

[Next question](#)

Amyloidosis is the least likely of the above options to result in a spastic paraparesis

### Spastic paraparesis

Spastic paraparesis describes a upper motor neuron pattern of weakness in the lower limbs

#### Causes

- demyelination e.g. multiple sclerosis
- cord compression: trauma, tumour
- parasagittal meningioma
- tropical spastic paraparesis
- transverse myelitis e.g. HIV
- syringomyelia
- hereditary spastic paraplegia
- osteoarthritis of the cervical spine

Which one of the following is most likely to cause a bilateral facial nerve palsy?

<input type="radio"/>	A. Acoustic neuroma
<input type="radio"/>	B. Cholesteatoma
<input type="radio"/>	C. Bell's palsy
<input type="radio"/>	D. Sarcoidosis
<input type="radio"/>	E. Amyloidosis

Next question

### Facial nerve

Supply - 'face, ear, taste, tear'

- face: muscles of facial expression
- ear: nerve to stapedius
- taste: supplies anterior two-thirds of tongue
- tear: parasympathetic fibres to lacrimal glands, also salivary glands

Causes of bilateral facial nerve palsy

- sarcoidosis
- Guillain-Barre syndrome
- polio, Lyme disease

Causes of unilateral facial nerve palsy - as above plus

Lower motor neuron	Upper motor neuron
<ul style="list-style-type: none"> <li>• Bell's palsy</li> <li>• Ramsay-Hunt syndrome (due to herpes zoster)</li> <li>• acoustic neuroma</li> <li>• parotid tumours</li> <li>• HIV</li> <li>• multiple sclerosis*</li> <li>• diabetes mellitus</li> </ul>	<ul style="list-style-type: none"> <li>• stroke</li> </ul>

LMN vs. UMN

- upper motor neuron lesion 'spares' upper face i.e. forehead
- lower motor neuron lesion affects all facial muscles

\*may also cause an UMN palsy

A 63-year-old man is prescribed ropinirole for Parkinson's disease. What is the mechanism of action?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. MAO-B inhibitor              |
| <input type="radio"/> | B. Antimuscarinic               |
| <input type="radio"/> | C. Dopamine receptor agonist    |
| <input type="radio"/> | D. Dopamine receptor antagonist |
| <input type="radio"/> | E. Decarboxylase inhibitor      |

Next question

Ropinirole - dopamine receptor agonist

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

## MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

## Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

## COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

## Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benztropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

A 59-year-old man with no significant past medical history is admitted to hospital following an ischaemic stroke. He presented outside of the thrombolysis window and is treated with aspirin for the first few days. His blood pressure is 130/80 mmHg, fasting glucose is 5.6 mmol/l and fasting cholesterol is 3.9 mmol/l. He makes a good recovery and has regained nearly all of his previous functions upon discharge. Following recent NICE guidelines, which of the following medications should he be taking upon discharge (i.e. after 14 days)?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Aspirin + statin                           |
| <input type="radio"/> | B. Aspirin + dipyridamole + statin + ramipril |
| <input type="radio"/> | C. Clopidogrel + statin                       |
| <input type="radio"/> | D. Aspirin + dipyridamole                     |
| <input type="radio"/> | E. Aspirin + dipyridamole + statin            |

[Next question](#)

### Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued stroke guidelines in 2008, although they modified their guidance with respect to antiplatelet therapy in 2010.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy\*
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commenced on a statin. Many physicians will delay treatment until after at least 48 hours due to the risk of haemorrhagic transformation

### Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 hours\*\* of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

## **Secondary prevention**

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- clopidogrel is now recommended by NICE ahead of combination use of aspirin plus modified release (MR) dipyridamole in people who have had an ischaemic stroke
- aspirin plus MR dipyridamole is now recommended after an ischaemic stroke only if clopidogrel is contraindicated or not tolerated, but treatment is no longer limited to 2 years' duration
- MR dipyridamole alone is recommended after an ischaemic stroke only if aspirin or clopidogrel are contraindicated or not tolerated, again with no limit on duration of treatment

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST\*\*\* criteria or > 50% according to NASCET\*\*\*\* criteria

\*the 2009 Controlling hypertension and hypotension immediately post-stroke (CHHIPS) trial may change thinking on this but guidelines have yet to change to reflect this

\*\*SIGN recommend a window of 4.5 hours

\*\*\*European Carotid Surgery Trialists' Collaborative Group

\*\*\*\*North American Symptomatic Carotid Endarterectomy Trial

Which one of the following infections is most strongly associated with the development of Guillain-Barre syndrome

<input type="radio"/>	A. <i>Shigella</i>
<input type="radio"/>	B. <i>Salmonella</i>
<input type="radio"/>	C. <i>E. coli</i> H7:0157
<input type="radio"/>	D. Herpes simplex
<input type="radio"/>	E. <i>Campylobacter jejuni</i>

Next question

*Campylobacter jejuni* is strongly associated with the development of Guillain-Barre syndrome

### Guillain-Barre syndrome

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*)

#### Pathogenesis

- cross reaction of antibodies with gangliosides in the peripheral nervous system
- correlation between anti-ganglioside antibody (e.g. anti-GM1) and clinical features has been demonstrated
- anti-GM1 antibodies in 25% of patients

#### Miller Fisher syndrome

- variant of Guillain-Barre syndrome
- associated with ophthalmoplegia, areflexia and ataxia. The eye muscles are typically affected first
- usually presents as a descending paralysis rather than ascending as seen in other forms of Guillain-Barre syndrome
- anti-GQ1b antibodies are present in 90% of cases



Lateral medullary syndrome is caused by occlusion of which one of the following blood vessels?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Anterior inferior cerebellar artery  |
| <input type="radio"/> | B. Posterior cerebral artery            |
| <input type="radio"/> | C. Lateral sinus thrombosis             |
| <input type="radio"/> | D. Middle cerebral artery               |
| <input type="radio"/> | E. Posterior inferior cerebellar artery |

[Next question](#)

Lateral medullary syndrome - PICA lesion - cerebellar signs, contralateral sensory loss & ipsilateral Horner's

### Lateral medullary syndrome

Lateral medullary syndrome, also known as Wallenberg's syndrome, occurs following occlusion of the posterior inferior cerebellar artery

#### Cerebellar features

- ataxia
- nystagmus

#### Brainstem features

- ipsilateral: dysphagia, facial numbness, cranial nerve palsy e.g. Horner's
- contralateral: limb sensory loss

A 29-year-old female presents complaining of weakness in her arms, leading to increasing difficulties at work. On examination she has a bilateral ptosis and loss of the red-reflex in both eyes. Urine testing also reveals glycosuria. What is the most likely diagnosis?

- ☐ A. Myotonic dystrophy
- ☐ B. Homocystinuria
- ☐ C. Multiple sclerosis
- ☐ D. Myasthenia gravis
- ☐ E. HIV

[Next question](#)

#### Dystrophia myotonica - DM1

- distal weakness initially
- autosomal dominant
- diabetes
- dysarthria

These features are typical of myotonic dystrophy. The red-reflex is lost due to bilateral cataracts

#### Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

#### Genetics

- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	DM2
<ul style="list-style-type: none"> <li>- DMPK gene on chromosome 19</li> <li>- Distal weakness more prominent</li> </ul>	<ul style="list-style-type: none"> <li>- ZNF9 gene on chromosome 3</li> <li>- Proximal weakness more prominent</li> <li>- Severe congenital form not seen</li> </ul>

## General features

- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

## Other features

- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia

A 56-year-old man presents to the Emergency Department after developing trouble talking after waking up this morning. The symptoms are consistent with expressive dysphasia and lasted about 90 minutes before resolving completely. Neurological examination is unremarkable. A diagnosis of transient ischaemic attack (TIA) is made.

His past medical history includes ischaemic heart disease for which he is prescribed aspirin, simvastatin and atenolol. Which one of the following factors is most associated with an increased risk of going on to have a stroke?

<input type="radio"/>	A. History of ischaemic heart disease
<input type="radio"/>	B. History of aspirin use
<input type="radio"/>	C. Duration of this TIA
<input type="radio"/>	D. Expressive dysphasia during this TIA
<input type="radio"/>	E. His age

Next question

This TIA lasted greater than 60 minutes which scores 2 as part of the ABCD2 prognostic scoring system. It is therefore the most significant factor which would increase his risk of going on to have a stroke.

### Transient ischaemic attack

NICE issued updated guidelines relating to stroke and transient ischaemic attack (TIA) in 2008. They advocated the use of the ABCD2 prognostic score for risk stratifying patients who've had a suspected TIA:

	Criteria	Points
A	Age $\geq$ 60 years	1
B	Blood pressure $\geq$ 140/90 mmHg	1
C	Clinical features	
	- Unilateral weakness	2
	- Speech disturbance, no weakness	1
D	Duration of symptoms	
	- > 60 minutes	2
	- 10-59 minutes	1
	Patient has diabetes	1

This gives a total score ranging from 0 to 7. People who have had a suspected TIA who are at a higher risk of stroke (that is, with an ABCD2 score of 4 or above) should have:

- aspirin (300 mg daily) started immediately
- specialist assessment and investigation within 24 hours of onset of symptoms
- measures for secondary prevention introduced as soon as the diagnosis is confirmed, including discussion of individual risk factors

If the ABCD2 risk score is 3 or below:

- specialist assessment within 1 week of symptom onset, including decision

on brain imaging

- if vascular territory or pathology is uncertain, refer for brain imaging

People with crescendo TIAs (two or more episodes in a week) should be treated as being at high risk of stroke, even though they may have an ABCD2 score of 3 or below.

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- aspirin plus modified-release (MR) dipyridamole is still recommended as first choice for people who have had a TIA, but now there is no recommended limit on the duration of treatment. Clopidogrel is not recommended
- MR dipyridamole monotherapy is recommended after TIA only if aspirin is contraindicated or not tolerated, again with no limit on duration of treatment.

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST\* criteria or > 50% according to NASCET\*\* criteria

\*European Carotid Surgery Trialists' Collaborative Group

\*\*North American Symptomatic Carotid Endarterectomy Trial

A 14-year-old male is noted to have optic atrophy on fundoscopy. Neurological exam reveals dysarthric speech and nystagmus. Knee and ankle jerks are absent but there is an extensor plantar response. What is the likely diagnosis?

<input type="radio"/>	A. Leber's optic atrophy
<input type="radio"/>	B. Ataxic telangiectasia
<input type="radio"/>	C. Friedreich's ataxia
<input type="radio"/>	D. Subacute combined degeneration of the cord
<input type="radio"/>	E. Multiple sclerosis

[Next question](#)

Multiple sclerosis would be unlikely at this age

### Friedreich's ataxia

Friedreich's ataxia is the most common of the early-onset hereditary ataxias. It is an autosomal recessive, trinucleotide repeat disorder characterised by a GAA repeat in the X25 gene on chromosome 9 (frataxin). Friedreich's ataxia is unusual amongst trinucleotide repeat disorders in not demonstrating the phenomenon of anticipation

The typical age of onset is 10-15 years old. Gait ataxia is the most common presenting feature.

#### Neurological features

- absent ankle jerks/extensor plantars
- cerebellar ataxia
- optic atrophy
- spinocerebellar tract degeneration

#### Other features

- hypertrophic obstructive cardiomyopathy (90%, most common cause of death)
- diabetes mellitus (10-20%)
- high-arched palate

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Next

A 46-year-old female presents with a burning sensation over the antero-lateral aspect of her right thigh. A diagnosis of meralgia paraesthetica is suspected. Which nerve is most likely to be affected?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. Common peroneal nerve              |
| <input type="radio"/> | B. Anterior cutaneous nerve of thigh  |
| <input type="radio"/> | C. Posterior cutaneous nerve of thigh |
| <input type="radio"/> | D. Lateral cutaneous nerve of thigh   |
| <input type="radio"/> | E. Sciatic nerve                      |

Next question

Burning thigh pain - ? meralgia paraesthetica - lateral cutaneous nerve of thigh compression

**Meralgia paraesthetica**

## Basics

- caused by compression of lateral cutaneous nerve of thigh
- typically burning sensation over antero-lateral aspect of thigh

A 72-year-old man who is being treated for Parkinson's disease is reviewed. Which one of the following features should prompt you to consider an alternative diagnosis?

<input type="radio"/>	A. Micrographia
<input type="radio"/>	B. Impaired olfaction
<input type="radio"/>	C. REM sleep behaviour disorder
<input type="radio"/>	D. Diplopia
<input type="radio"/>	E. Psychosis

[Next question](#)

Diplopia is not common in Parkinson's disease and may suggest an alternative cause of parkinsonism such as progressive supranuclear palsy

### Parkinson's disease: features

Parkinson's disease is a progressive neurodegenerative condition caused by degeneration of dopaminergic neurons in the substantia nigra.. This results in a classic triad of features: bradykinesia, tremor and rigidity. The symptoms of Parkinson's disease are characteristically asymmetrical

#### Bradykinesia

- poverty of movement also seen: mask-like facies
- difficulty in initiating movement

#### Tremor

- most marked at rest, 3-5 Hz
- typically 'pill-rolling'

#### Rigidity

- lead pipe
- cogwheel: due to superimposed tremor

#### Other characteristic features

- flexed posture
- short, shuffling steps
- micrographia
- drooling of saliva



- psychiatric features: depression is the most common feature (affects about 40%); dementia, psychosis and sleep disturbances may also occur
- impaired olfaction
- REM sleep behaviour disorder

**Drug-induced parkinsonism** has slightly different features to Parkinson's disease:

- motor symptoms are generally rapid onset and bilateral
- rigidity and rest tremor are uncommon

A 52-year-old woman presents with a two week history of dizziness when she rolls over in bed. She says it feels like the room is spinning around her. Examination of her ears and cranial nerves is unremarkable. Given the likely diagnosis of benign paroxysmal positional vertigo what is the most appropriate management?

<input type="radio"/>	A. Trial of prochlorperazine
<input type="radio"/>	B. Request MRI brain
<input type="radio"/>	C. Advise review by an optician
<input type="radio"/>	D. Perform Epley manoeuvre
<input type="radio"/>	E. Trial of cinnarizine

[Next question](#)

### Benign paroxysmal positional vertigo

Benign paroxysmal positional vertigo (BPPV) is one of the most common causes of vertigo encountered. It is characterised by the sudden onset of dizziness and vertigo triggered by changes in head position

#### Features

- vertigo triggered by change in head position (e.g. rolling over in bed or gazing upwards)
- may be associated with nausea
- each episode typically lasts 10-20 seconds
- positive Halpike manoeuvre

BPPV has a good prognosis and usually resolves spontaneously after a few weeks to months. Symptomatic relief may be gained by:

- Epley manoeuvre (successful in around 80% of cases)
- teaching the patient exercises they can do themselves at home, for example Brandt-Daroff exercises

Medication is often prescribed (e.g. Betahistine) but it tends to be of limited value

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Next

A 62-year-old man is referred to the neurology clinic with worsening symptoms over the past few months. The neurologist suspects the patient has progressive supranuclear palsy. Which one of the following features is least likely to be seen in this patient?

<input type="radio"/>	A. Poor response to L-dopa
<input type="radio"/>	B. Impairment of horizontal gaze
<input type="radio"/>	C. Falls
<input type="radio"/>	D. Cognitive impairment
<input type="radio"/>	E. Slurring of speech

Next question

Progressive supranuclear palsy: parkinsonism, impairment of vertical gaze

Impairment of vertical gaze is seen in progressive supranuclear palsy. Horizontal gaze impairment is sometimes seen later as the disease progresses, but would be atypical in a newly diagnosed patient.

**Progressive supranuclear palsy**

## Overview

- aka Steele-Richardson-Olszewski syndrome
- a 'Parkinson Plus' syndrome

## Features

- impairment of vertical gaze (down gaze worse than up gaze - patients may complain of difficulty reading or descending stairs)
- parkinsonism
- falls
- slurring of speech
- cognitive impairment

## Management

- poor response to L-dopa

A 56-year-old woman comes for review. Around 4 weeks ago she had a blistering rash under her right breast which extended around to the back. A diagnosis of shingles was made. Unfortunately since that time she has been experiencing severe 'shooting' pains. The skin is also very tender to touch. Neither paracetamol nor ibuprofen have helped her symptoms. What is the most appropriate next step in management?

- |                       |                    |
|-----------------------|--------------------|
| <input type="radio"/> | A. Lidocaine patch |
| <input type="radio"/> | B. Tramadol        |
| <input type="radio"/> | C. Amitriptyline   |
| <input type="radio"/> | D. Carbamazepine   |
| <input type="radio"/> | E. Diclofenac      |

[Next question](#)

This lady has developed post-herpetic neuralgia. NICE recommend using amitriptyline or pregabalin first-line.

### Neuropathic pain

Neuropathic pain may be defined as pain which arises following damage or disruption of the nervous system. It is often difficult to treat and responds poorly to standard analgesia.

Examples include:

- diabetic neuropathy
- post-herpetic neuralgia
- trigeminal neuralgia
- prolapsed intervertebral disc

NICE issued guidance in 2010 on the management of neuropathic pain:

- first-line treatment\*: oral amitriptyline or pregabalin
- if satisfactory pain reduction is obtained with amitriptyline but the person cannot tolerate the adverse effects, consider oral imipramine or nortriptyline as an alternative
- second-line treatment: if first-line treatment was with amitriptyline, switch to or combine with pregabalin. If first-line treatment was with pregabalin, switch to or

combine with amitriptyline

- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

\*please note that for some specific conditions the guidance may vary. For example carbamazepine is used first-line for trigeminal neuralgia, duloxetine for diabetic neuropathy

A patient is noted to have absent ankle jerks combined with extensor plantars on examination. Which one of the following is least likely?

<input type="radio"/>	A. Multiple sclerosis
<input type="radio"/>	B. Subacute combined degeneration of the cord
<input type="radio"/>	C. Syringomyelia
<input type="radio"/>	D. Syphilis
<input type="radio"/>	E. Motor neuron disease

[Next question](#)

Multiple sclerosis would not give this combination of physical signs

### Absent ankle jerks, extensor plantars

Typically caused by lesion producing both upper motor neuron (extensor plantars) and lower motor neuron (absent ankle jerk) signs

#### Causes

- subacute combined degeneration of the cord
- motor neuron disease
- Friedreich's ataxia
- syringomyelia
- taboparesis (syphilis)
- conus medullaris lesion

A 42-year-old woman presents as she has noticed a 'droop' in the right side of her face since she woke up this morning. There is no associated limb weakness, dysphagia or visual disturbance. On examination you notice right-sided upper and lower facial paralysis. Which one of the following features would be most consistent with a diagnosis of Bell's palsy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Vesicular rash around the ear                          |
| <input type="radio"/> | B. Hyperacusis  |
| <input type="radio"/> | C. Sensory loss over the distribution of the facial nerve |
| <input type="radio"/> | D. Pins and needles in the right arm                      |
| <input type="radio"/> | E. Rhinorrhoea  |

[Next question](#)

A vesicular rash around the ear would suggest a diagnosis of Ramsey Hunt syndrome. Hyperacusis is seen in around a third of patients.

### Bell's palsy

Bell's palsy may be defined as an acute, unilateral, idiopathic, facial nerve paralysis. The aetiology is unknown although the role of the herpes simplex virus has been investigated previously.

#### Features

- lower motor neuron facial nerve palsy - forehead affected\*
- patients may also notice post-auricular pain (may precede paralysis), altered taste, dry eyes, hyperacusis

#### Management

- in the past a variety of treatment options have been proposed including no treatment, prednisolone only and a combination of aciclovir and prednisolone
- following a National Institute for Health randomised controlled trial it is now recommended that prednisolone 25mg bd for 10 days should be prescribed for patients within 72 hours of onset of Bell's palsy. Adding in aciclovir gives no additional benefit
- eye care is important - prescription of artificial tears and eye lubricants should be considered

#### Prognosis

- if untreated around 15% of patients have permanent moderate to severe weakness

\*upper motor neuron lesion 'spares' upper face

A 47-year-old man presents to the Emergency Department with a three day history of severe headache associated with vomiting. There is no past medical history of note. On examination blood pressure is 98/62 mmHg, pulse is 108 bpm and temperature is 37.0°C. There is mild neck stiffness and a partial third nerve palsy of the left eye. Blood tests reveal:

Hb	14.8 g/dl
Plt	$373 \times 10^9/l$
WBC	$13.6 \times 10^9/l$
Na <sup>+</sup>	132 mmol/l
K <sup>+</sup>	5.2 mmol/l
Urea	4.2 mmol/l
Creatinine	99 µmol/l
Free T4	9 pmol/l (range 10-22)

What is the most likely diagnosis?

<input type="radio"/>	A. Subarachnoid haemorrhage
<input type="radio"/>	B. Cavernous sinus thrombosis
<input type="radio"/>	C. Meningitis
<input type="radio"/>	D. Pituitary apoplexy
<input type="radio"/>	E. Lateral sinus thrombosis

Next question

The hypotension, electrolytes and low free T4 point towards hypopituitarism. Clinically, pituitary apoplexy can mimic a subarachnoid haemorrhage

### Pituitary apoplexy

Sudden enlargement of pituitary tumour secondary to haemorrhage or infarction

#### Features

- sudden onset headache similar to that seen in subarachnoid haemorrhage
- vomiting
- neck stiffness
- visual field defects: classically bitemporal superior quadrantic defect
- extraocular nerve palsies
- features of pituitary insufficiency e.g. Hypotension secondary to hypoadrenalism

Which one of the following is a contraindication to the use of a triptan in the management of migraine?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Concurrent pizotifen use             |
| <input type="radio"/> | B. Patients older than 55 years         |
| <input type="radio"/> | C. A history of epilepsy                |
| <input type="radio"/> | D. Previous intracranial tumour         |
| <input type="radio"/> | E. A history of ischaemic heart disease |

Next question

## Triptans

Triptans are specific 5-HT<sub>1</sub> agonists used in the acute treatment of migraine. They are generally used second line when standard analgesics such as paracetamol and ibuprofen are ineffective.

### Prescribing points

- should be taken as soon as possible after the onset of headache, rather than at onset of aura
- oral, orodispersible, nasal spray and subcutaneous injections are available

### Adverse effects

- 'triptan sensations' - tingling, heat, tightness (e.g. throat and chest), heaviness, pressure

### Contraindications

- patients with a history of, or significant risk factors for, ischaemic heart disease or cerebrovascular disease



A 24-year-old man is seen in the 'First Seizure' clinic. He has been referred by the local the Emergency Department following a single episode of a witnessed seizure. Which one of the following factors would be least relevant when deciding whether to start anti-epileptic drugs after a single seizure?

<input type="radio"/>	A. Brain imaging shows a structural abnormality
<input type="radio"/>	B. The patient has a neurological deficit
<input type="radio"/>	C. The EEG shows unequivocal epileptic activity
<input type="radio"/>	D. The patient is less than 45 years old
<input type="radio"/>	E. The patient considers the risk of having a further seizure unacceptable

[Next question](#)

### Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Generalised tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures\* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

## Partial seizures

- carbamazepine
- second line: lamotrigine\*\*, sodium valproate

\*carbamazepine may actually exacerbate absence seizure

\*\*the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

A 23-year-old man is admitted following the sudden onset of an occipital headache. On examination GCS is 15/15, neurological examination is unremarkable but neck stiffness is noted. A subarachnoid haemorrhage is suspected but the CT scan is normal. At what time should a lumbar puncture be done to exclude the diagnosis?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Immediately            |
| <input type="radio"/> | B. 2 hours post-headache  |
| <input type="radio"/> | C. 4 hours post-headache  |
| <input type="radio"/> | D. 12 hours post-headache |
| <input type="radio"/> | E. 24 hours post-headache |

Next question

If the patient was acutely unwell or had an altered GCS then discussion with neurosurgery may be appropriate rather than waiting 12 hours

### Subarachnoid haemorrhage

#### Causes

- 85% are due to rupture of berry aneurysms (conditions associated with berry aneurysms include adult polycystic kidney disease, Ehlers-Danlos syndrome and coarctation of the aorta)
- AV malformations
- trauma
- tumours

#### Investigations

- CT: negative in 5%
- LP: done after 12 hrs (allowing time for xanthochromia to develop)

#### Complications

- rebleeding (in 30%)
- obstructive hydrocephalus (due to blood in ventricles)
- vasospasm leading to cerebral ischaemia

#### Management

- neurosurgical opinion: no clear evidence over early surgical intervention against delayed intervention
- nimodipine (e.g. 60mg / 4 hrly, if BP allows) has been shown to reduce the severity of neurological deficits but doesn't reduce rebleeding\*

\*the way nimodipine works in subarachnoid haemorrhage is not fully understood. It has been previously postulated that it reduces cerebral vasospasm (hence maintaining cerebral perfusion) but this has not been demonstrated in studies

Which one of the following causes of peripheral neuropathy is most associated with demyelination?

<input type="radio"/>	A. Vasculitis
<input type="radio"/>	B. Alcohol
<input type="radio"/>	C. Hereditary sensorimotor neuropathies (HSMN) type I
<input type="radio"/>	D. Vitamin B12 deficiency
<input type="radio"/>	E. Diabetes mellitus

Next question

### Peripheral neuropathy: demyelinating vs. axonal

#### Demyelinating pathology

- Guillain-Barre syndrome
- chronic inflammatory demyelinating polyneuropathy (CIDP)
- amiodarone
- hereditary sensorimotor neuropathies (HSMN) type I
- paraprotein neuropathy

#### Axonal pathology

- alcohol
- diabetes mellitus\*
- vasculitis
- vitamin B12 deficiency\*
- hereditary sensorimotor neuropathies (HSMN) type II

\* may also cause a demyelinating picture

A 19-year-old man is admitted following a generalised seizure. No past history is available as the man is currently in a postictal state. On examination it is noted that he has three patches of hypopigmented skin and fibromata under two of his finger nails. What is the most likely diagnosis?

<input type="radio"/>	A. Neurofibromatosis
<input type="radio"/>	B. Lennox-Gastaut Syndrome
<input type="radio"/>	C. Multiple endocrine neoplasia type 1
<input type="radio"/>	D. Birt-Hogg-Dube syndrome
<input type="radio"/>	E. Tuberous sclerosis

Next question

This man has a neurocutaneous syndrome which raises the possibility of neurofibromatosis or tuberous sclerosis. Given the areas of hypopigmentation and subungual fibromas the most likely diagnosis is tuberous sclerosis

### Tuberous sclerosis

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous

#### Cutaneous features

- depigmented 'ash-leaf' spots which fluoresce under UV light
- roughened patches of skin over lumbar spine (Shagreen patches)
- adenoma sebaceum: butterfly distribution over nose
- fibromata beneath nails (subungual fibromata)
- café-au-lait spots\* may be seen

#### Neurological features

- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment

#### Also

- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- gliomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata

\*these of course are more commonly associated with neurofibromatosis. However a 1998 study of 106 children with TS found café-au-lait spots in 28% of patients

A 45-year-old woman presents complaining of visual disturbance. Examination reveals a left congruous homonymous hemianopia. Where is the lesion most likely to be?

<input type="radio"/>	A. Optic chiasm
<input type="radio"/>	B. Left occipital cortex
<input type="radio"/>	C. Right optic tract
<input type="radio"/>	D. Right occipital cortex
<input type="radio"/>	E. Left optic tract

Next question

Visual field defects:

- left homonymous hemianopia means visual field defect to the left, i.e. lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

### Visual field defects

The main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

A congruous defect simply means complete or symmetrical visual field loss and conversely an incongruous defect is incomplete or asymmetric. Please see the link for an excellent diagram.

Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias\*

- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe

- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

#### Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

\*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details:

<http://www.ncbi.nlm.nih.gov/pubmed/9109741>



A 5-year-old boy is diagnosed as having absence seizures. What is the chance he will be seizure free by the age of 16-years-old?

<input type="radio"/>	A. 5-10%
<input type="radio"/>	B. 20-25%
<input type="radio"/>	C. 40-45%
<input type="radio"/>	D. 65-70%
<input type="radio"/>	E. 90-95%

[Next question](#)

Absence seizures - good prognosis: 90-95% become seizure free in adolescence

## Absence seizures

Absence seizures (petit mal) are a form of generalised epilepsy that is mostly seen in children. The typical age of onset of 3-10 years old and girls are affected twice as commonly as boys

### Features

- absences last a few seconds and are associated with a quick recovery
- seizures may be provoked by hyperventilation or stress
- the child is usually unaware of the seizure
- they may occur many times a day
- EEG: bilateral, symmetrical 3Hz spike and wave pattern

### Management

- sodium valproate and ethosuximide are first-line treatment
- good prognosis - 90-95% become seizure free in adolescence

A 67-year-old man is reviewed in the neurology clinic due to concerns about increasing clumsiness. Examination reveals an ataxic gait and increased upper limb tone with cog-wheel rigidity. Blood pressure is 135/80 lying and 95/70 standing. What is the most likely diagnosis?

<input type="radio"/>	A. Motor neuron disease
<input type="radio"/>	B. Progressive supranuclear palsy
<input type="radio"/>	C. Parkinson's disease
<input type="radio"/>	D. Multiple sclerosis
<input type="radio"/>	E. Multiple system atrophy

[Next question](#)

Whilst postural hypotension may be seen in Parkinson's disease the ataxic gait point towards a diagnosis of multiple system atrophy.

### Multiple system atrophy

Shy-Drager syndrome is a type of multiple system atrophy

#### Features

- parkinsonism
- autonomic disturbance (atonic bladder, postural hypotension)
- cerebellar signs

A 66-year-old woman is investigated for ascites and found to have ovarian cancer. She presents due to 'unsteadiness'. On examination there is evidence of nystagmus and past-pointing. Which one of the following antibodies is most likely to be present?

<input type="radio"/>	A. Anti-Hu
<input type="radio"/>	B. Anti-Yo
<input type="radio"/>	C. Anti-Ri
<input type="radio"/>	D. Anti-Ro
<input type="radio"/>	E. Anti-La

[Next question](#)

This lady has developed cerebellar syndrome secondary to anti-Yo antibodies.

### Paraneoplastic syndromes affecting nervous system

#### Lambert-Eaton myasthenic syndrome

- associated with small cell lung cancer (also breast and ovarian)
- antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system
- can also occur independently as autoimmune disorder

#### Anti-Hu

- associated with small cell lung carcinoma and neuroblastomas
- sensory neuropathy - may be painful
- cerebellar syndrome
- encephalomyelitis

#### Anti-Yo

- associated with ovarian and breast cancer
- cerebellar syndrome

#### Anti-GAD antibody

- associated with breast, colorectal and small cell lung carcinoma
- stiff person's syndrome or diffuse hypertonia

#### Anti-Ri

- associated with breast and small cell lung carcinoma
- ocular opsoclonus-myoclonus

Which one of the following is least recognised as a cause of autonomic neuropathy

<input type="radio"/>	A. Guillain-Barre syndrome
<input type="radio"/>	B. New variant CJD
<input type="radio"/>	C. Diabetes
<input type="radio"/>	D. Parkinson's
<input type="radio"/>	E. HIV

Next question

## Autonomic neuropathy

### Features

- impotence, inability to sweat, postural hypotension
- postural hypotension e.g. drop of 30/15 mmHg
- loss of decrease in heart rate following deep breathing
- pupils: dilates following adrenaline instillation

### Causes

- diabetes
- Guillain-Barre syndrome
- multisystem atrophy (MSA), Shy-Drager syndrome
- Parkinson's
- infections: HIV, Chagas' disease, neurosyphilis
- drugs: antihypertensives, tricyclics
- craniopharyngioma

A 29-year-old female presents complaining of double vision and unsteadiness. She has no past medical history of note. On examination she has limited movement of her eyes in all directions. Pupils are 3 mm, equal and reactive to light. Examination of the peripheral nervous system is normal other than reduced reflexes and the plantars are down going. Some past-pointing is also noted. What is the most likely diagnosis?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Multiple sclerosis     |
| <input type="radio"/> | B. Conversion disorder    |
| <input type="radio"/> | C. Miller Fisher syndrome |
| <input type="radio"/> | D. Ataxic telangiectasia  |
| <input type="radio"/> | E. Friedreich's ataxia    |

Next question

Miller Fisher syndrome - areflexia, ataxia, ophthalmoplegia

This patient has Miller Fisher syndrome, a variant of Guillain-Barre syndrome

### Guillain-Barre syndrome

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*)

#### Pathogenesis

- cross reaction of antibodies with gangliosides in the peripheral nervous system
- correlation between anti-ganglioside antibody (e.g. anti-GM1) and clinical features has been demonstrated
- anti-GM1 antibodies in 25% of patients

#### Miller Fisher syndrome

- variant of Guillain-Barre syndrome
- associated with ophthalmoplegia, areflexia and ataxia. The eye muscles are typically affected first
- usually presents as a descending paralysis rather than ascending as seen in other forms of Guillain-Barre syndrome
- anti-GQ1b antibodies are present in 90% of cases

In the treatment of migraine, sumatriptan is an example of a:

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Beta-blocker  |
| <input type="radio"/> | B. Alpha-blocker and a partial 5-HT <sub>2</sub> agonist |
| <input type="radio"/> | C. Specific 5-HT <sub>1</sub> agonist                    |
| <input type="radio"/> | D. 5-HT <sub>2</sub> antagonist                          |
| <input type="radio"/> | E. Tricyclic antidepressant                              |

Next question

### Migraine

- acute: triptan + NSAID or triptan + paracetamol
- prophylaxis: topiramate or propranolol

### Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. NICE produced guidelines in 2012 on the management of headache, including migraines.

#### Acute treatment

- first-line: offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol
- for young people aged 12-17 years consider a nasal triptan in preference to an oral triptan
- if the above measures are not effective or not tolerated offer a non-oral preparation of metoclopramide\* or prochlorperazine and consider adding a non-oral NSAID or triptan

#### Prophylaxis

- prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients.
- NICE advise either topiramate or propranolol 'according to the person's preference, comorbidities and risk of adverse events'. Propranolol should be used in preference to topiramate in women of child bearing age as it may be teratogenic and it can reduce the effectiveness of hormonal contraceptives
- if these measures fail NICE recommend 'a course of up to 10 sessions of acupuncture over 5-8 weeks' or gabapentin

- NICE recommend: 'Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people'
- for women with predictable menstrual migraine treatment NICE recommend either frovatriptan (2.5 mg twice a day) or zolmitriptan (2.5 mg twice or three times a day) as a type of 'mini-prophylaxis'
- pizotifen is no longer recommend. Adverse effects such as weight gain & drowsiness are common

\*caution should be exercised with young patients as acute dystonic reactions may develop

A 34-year-old female is reviewed in the neurology clinic due to a number of 'funny-dos'. She describes a sensation that her surroundings are unreal, 'like a dream'. Following this she has been told that she starts to smack her lips, although she has no recollection of doing this. What is the most likely diagnosis?

<input type="radio"/>	A. Myoclonic seizure
<input type="radio"/>	B. Simple partial seizure
<input type="radio"/>	C. Complex partial seizure
<input type="radio"/>	D. Partial seizure progressing to generalised seizure
<input type="radio"/>	E. Absence seizure

[Next question](#)

With simple partial seizures there is no disturbance of consciousness or awareness. Lip smacking is an example of an automatism - an automatic, repetitive act

## Epilepsy: classification

### Basics

- two main categories are generalised and partial seizures
- partial seizures may progress to general seizures
- other types: myoclonic, atypical absence, atonic and tonic seizures are usually seen in childhood

Generalised - no focal features, consciousness lost immediately

- grand mal (tonic-clonic)
- petit mal (absence seizures)
- partial seizures progressing to generalised seizures

Partial - focal features depending on location

- simple (no disturbance of consciousness or awareness)
- complex (consciousness is disturbed)
- temporal lobe --> aura, déjà vu, jamais vu; motor --> Jacksonian

### Myoclonus

- occur in a variety of conditions



A 25-year-old female presents 5 days after discharge from hospital following an admission for suspected meningitis. A lumbar puncture was performed which showed no evidence of infection. Unfortunately she developed a headache 48 hours after discharge. This has now lasted 3 days and has failed to settle with analgesia. Which one of the following treatment options should be considered?

- ☐ A. Intrathecal steroids
- ☐ B. Repeat lumbar puncture
- ☐ C. Course of oral prednisolone
- ☐ D. Blood patch
- ☐ E. Intravenous fluids on top of oral fluid intake

Next question

### Post-lumbar puncture headache

Headache following lumbar puncture (LP) occurs in approximately one-third of patients. The pathophysiology of is unclear but may relate to a 'leak' of CSF following dural puncture. Post-LP headaches are more common in young females with a low body mass index

#### Typical features

- usually develops within 24-48 hours following LP but may occur up to one week later
- may last several days
- worsens with upright position
- improves with recumbent position

Factors which may contribute to headache	Factors which do not contribute to headache
Increased needle size Direction of bevel Not replacing the stylet Increased number of LP attempts	Increased volume of CSF removed Bed rest following procedure Increased fluid intake post procedure Opening pressure of CSF Position of patient

#### Management

- supportive initially (analgesia, rest)
- if pain continues for more than 72 hours then specific treatment is indicated, to prevent subdural haematoma
- treatment options include: blood patch, epidural saline and intravenous caffeine

A 62-year-old man presents with left-sided eye pain and diplopia for the past 2 days. Examination of his eyes shows his pupils equal and reactive to light with no proptosis. There is however an apparent palsy of the 6th cranial nerve associated with a partial 3rd nerve palsy on the left side. Examining the remaining cranial demonstrates hyperaesthesia of the upper face on the left side. Where is the likely lesion?

<input type="radio"/>	A. Cavernous sinus
<input type="radio"/>	B. Orbital apex
<input type="radio"/>	C. Pons
<input type="radio"/>	D. Cerebropontine angle
<input type="radio"/>	E. Medulla

[Next question](#)

## Intracranial venous thrombosis

### Overview

- can cause cerebral infarction, much less common than arterial causes
- 50% of patients have isolated sagittal sinus thromboses - the remainder have coexistent lateral sinus thromboses and cavernous sinus thromboses

### Features

- headache (may be sudden onset)
- nausea & vomiting

### Sagittal sinus thrombosis

- may present with seizures and hemiplegia
- parasagittal biparietal or bifrontal haemorrhagic infarctions are sometimes seen

### Cavernous sinus thrombosis

- other causes of cavernous sinus syndrome: local infection (e.g. sinusitis), neoplasia, trauma
- periorbital oedema
- ophthalmoplegia: 6th nerve damage typically occurs before 3rd & 4th
- trigeminal nerve involvement may lead to hyperaesthesia of upper face and eye pain
- central retinal vein thrombosis

### Lateral sinus thrombosis

- 6th and 7th cranial nerve palsies

A 29-year-old man with a history of schizophrenia is taken to the local Emergency Department as he is generally unwell. He is currently taking olanzapine and citalopram. On examination he is noted to have a temperature of 37.0°C and his blood pressure is 170/100 mmHg. Which other examination finding would best support a diagnosis of neuroleptic malignant syndrome?

- |                       |                    |
|-----------------------|--------------------|
| <input type="radio"/> | A. Ataxia          |
| <input type="radio"/> | B. Hyperreflexia   |
| <input type="radio"/> | C. Muscle rigidity |
| <input type="radio"/> | D. Tremor          |
| <input type="radio"/> | E. Papilloedema    |

[Next question](#)

### Neuroleptic malignant syndrome

Neuroleptic malignant syndrome is a rare but dangerous condition seen in patients taking antipsychotic medication. It carries a mortality of up to 10% and can also occur with atypical antipsychotics

#### Features

- more common in young male patients
- onset usually in first 10 days of treatment or after increasing dose
- pyrexia
- rigidity
- tachycardia

A raised creatine kinase is present in most cases. A leukocytosis may also be seen

#### Management

- stop antipsychotic
- IV fluids to prevent renal failure
- dantrolene may be useful in selected cases
- bromocriptine, dopamine agonist, may also be used

Which one of the following side-effects is least associated with the use of levodopa?

<input type="radio"/>	A. Psychosis
<input type="radio"/>	B. 'On-off' effect
<input type="radio"/>	C. Postural hypotension
<input type="radio"/>	D. Cardiac arrhythmias
<input type="radio"/>	E. Galactorrhoea

Next question

## Levodopa

### Overview

- usually combined with a decarboxylase inhibitor (e.g. carbidopa or benserazide) to prevent peripheral metabolism of L-dopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- no use in neuroleptic induced parkinsonism

### Adverse effects

- dyskinesia
- 'on-off' effect
- postural hypotension
- cardiac arrhythmias
- nausea & vomiting
- psychosis
- reddish discolouration of urine upon standing

Which one of the following is not a recognised causes of miosis?

<input type="radio"/>	A. Old age
<input type="radio"/>	B. Pontine haemorrhage
<input type="radio"/>	C. Holmes-Adie pupil
<input type="radio"/>	D. Argyll-Robertson pupil
<input type="radio"/>	E. Horner's syndrome

Next question

Holmes-Adie pupil is a benign condition most commonly seen in women. It is one of the differentials of a dilated pupil

### Miosis

Causes of miosis (small pupil)

- Horner's syndrome
- Argyll-Robertson pupil
- senile miosis
- pontine haemorrhage
- congenital

Drugs causes

- opiates
- parasympathomimetics: pilocarpine
- organophosphate toxicity

Which of the following drugs is least likely to cause peripheral neuropathy?

<input type="radio"/>	A. Amiodarone
<input type="radio"/>	B. Vincristine
<input type="radio"/>	C. Trimethoprim
<input type="radio"/>	D. Isoniazid
<input type="radio"/>	E. Nitrofurantoin

Next question

Trimethoprim is not listed in the BNF as causing peripheral neuropathy

### Drugs causing peripheral neuropathy

Drugs causing a peripheral neuropathy

- antibiotics: nitrofurantoin, metronidazole
- amiodarone
- isoniazid
- vincristine
- tricyclic antidepressants

A 23-year-old man with difficult to control epilepsy is reviewed in clinic, four months after a change in his antiepileptic medication. He has remained seizure free but has gained 5 kg in weight since last reviewed. Which one of the following antiepileptic drugs is most associated with weight gain?

<input type="radio"/>	A. Ethosuximide
<input type="radio"/>	B. Sodium valproate
<input type="radio"/>	C. Levetiracetam
<input type="radio"/>	D. Carbamazepine
<input type="radio"/>	E. Lamotrigine

[Next question](#)

### Sodium valproate

Sodium valproate is used in the management of epilepsy and is first line therapy for generalised seizures. It works by increasing GABA activity.

#### Adverse effects

- gastrointestinal: nausea
- increased appetite and weight gain
- alopecia: regrowth may be curly
- ataxia
- tremor
- hepatitis
- pancreatitis
- thrombocytopaenia
- teratogenic

### Question 101 of 204

Next

A 15-year-old boy is reviewed. He has been referred by his GP with ptosis, diplopia and night blindness. On examination he is noted to have a degree of ophthalmoplegia, bilateral partial ptosis and evidence of retinitis pigmentosa during fundoscopy. His mother developed a similar problem when she was 18-years-old. What is the most likely diagnosis?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Kearns-Sayre syndrome        |
| <input type="radio"/> | B. Alport's syndrome            |
| <input type="radio"/> | C. Usher syndrome               |
| <input type="radio"/> | D. Refsum disease               |
| <input type="radio"/> | E. Lawrence-Moon-Biedl syndrome |

Next question

#### Kearns-Sayre syndrome

- mitochondrial inheritance
- onset < 20-years-old
- external ophthalmoplegia
- retinitis pigmentosa

### Mitochondrial diseases

Whilst most DNA is found in the cell nucleus, a small amount of double-stranded DNA is present in the mitochondria. It encodes protein components of the respiratory chain and some special types of RNA

Mitochondrial inheritance has the following characteristics:

- inheritance is only via the maternal line as the sperm contributes no cytoplasm to the zygote
- all children of affected males will not inherit the disease
- all children of affected females will inherit it
- generally encode rare neurological diseases
- poor genotype:phenotype correlation - within a tissue or cell there can be different mitochondrial populations - this is known as heteroplasmy)

#### Histology

- muscle biopsy classically shows 'red, ragged fibres' due to increased number of mitochondria



Examples include:

- Leber's optic atrophy
- MELAS syndrome: mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes
- MERRF syndrome: myoclonus epilepsy with ragged-red fibres
- Kearns-Sayre syndrome: onset in patients < 20 years old, external ophthalmoplegia, retinitis pigmentosa.  
Ptosis may be seen
- sensorineural hearing loss

A 34-year-old female with a history of primary generalised epilepsy asks for advice in the neurology clinic as she plans to start a family. She currently takes sodium valproate as monotherapy. What advice should be given regarding the prevention of neural tube defects?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Folic acid 400 mcg per day once pregnancy has been confirmed |
| <input type="radio"/> | B. Folic acid 1 mg per day once pregnancy has been confirmed    |
| <input type="radio"/> | C. Folic acid 5 mg per day starting now                         |
| <input type="radio"/> | D. Folic acid 10 mg per day starting now                        |
| <input type="radio"/> | E. Folic acid 400 mcg per day starting now                      |

[Next question](#)

Epilepsy + pregnancy = 5mg folic acid

### Epilepsy: pregnancy and breast feeding

The risks of uncontrolled epilepsy during pregnancy generally outweigh the risks of medication to the fetus. All women thinking about becoming pregnant should be advised to take folic acid 5mg per day well before pregnancy to minimise the risk of neural tube defects. Around 1-2% of newborns born to non-epileptic mothers have congenital defects. This rises to 3-4% if the mother takes antiepileptic medication.

#### Other points

- aim for monotherapy
- there is no indication to monitor antiepileptic drug levels
- sodium valproate: associated with neural tube defects
- carbamazepine: often considered the least teratogenic of the older antiepileptics
- phenytoin: associated with cleft palate
- lamotrigine: studies to date suggest the rate of congenital malformations may be low. The dose of lamotrigine may need to be increased in pregnancy

Breast feeding is generally considered safe for mothers taking antiepileptics with the possible exception of the barbiturates

It is advised that pregnant women taking phenytoin are given vitamin K in the last month of pregnancy to prevent clotting disorders in the newborn

Which one of the following is least likely to cause a raised protein level in the cerebrospinal fluid?

<input type="radio"/>	A. Tuberculous meningitis
<input type="radio"/>	B. Guillain-Barre syndrome
<input type="radio"/>	C. Fungal meningitis
<input type="radio"/>	D. Spinal block
<input type="radio"/>	E. Systemic lupus erythematosus

Next question

### Cerebrospinal fluid: raised protein

Normal values of cerebrospinal fluid (CSF) are as follows:

- pressure = 60-150 mm (patient recumbent)
- protein = 0.2-0.4 g/l
- glucose =  $> 2/3$  blood glucose
- cells: red cells = 0, white cells  $< 5/\text{mm}^3$

The following conditions are associated with raised protein levels

- Guillain-Barre syndrome
- tuberculous, fungal and bacterial meningitis
- spinal block (Froin's syndrome\*)
- viral encephalitis

\*describes an increase in CSF protein below a spinal canal blockage (e.g. tumour, disc, infection)

Which one of the following features is most associated with parietal lobe lesions?

<input type="radio"/>	A. Gerstmann's syndrome
<input type="radio"/>	B. Perseveration
<input type="radio"/>	C. Cortical blindness
<input type="radio"/>	D. Superior homonymous quadrantanopia
<input type="radio"/>	E. Wernicke's aphasia

Next question

## Brain lesions

The following neurological disorders/features may allow localisation of a brain lesion:

### Gross anatomy

#### Parietal lobe lesions

- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

#### Occipital lobe lesions

- homonymous hemianopia (with macula sparing)
- cortical blindness
- visual agnosia

#### Temporal lobe lesion

- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia
- prosopagnosia (difficulty recognising faces)

#### Frontal lobes lesions

- expressive (Broca's) aphasia: located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus
- disinhibition
- perseveration
- anosmia
- inability to generate a list

## Cerebellum lesions

- midline lesions: gait and truncal ataxia
- hemisphere lesions: intention tremor, past pointing, dysdiadokinesis, nystagmus

## More specific areas

Medial thalamus and mammillary bodies of the hypothalamus	Wernicke and Korsakoff syndrome
Subthalamic nucleus of the basal ganglia	Hemiballism
Striatum (caudate nucleus) of the basal ganglia	Huntington chorea
Substantia nigra of the basal ganglia	Parkinson's disease
Amygdala	KluverBucy syndrome (hypersexuality, hyperorality, hyperphagia, visual agnosia)

You are asked to perform a neurological exam of the lower limbs on a patient with multiple sclerosis. Which one of the following findings is least typical?

<input type="radio"/>	A. Decreased tone
<input type="radio"/>	B. Patellar clonus
<input type="radio"/>	C. Upgoing plantars
<input type="radio"/>	D. Weakness
<input type="radio"/>	E. Brisk reflexes

[Next question](#)

In multiple sclerosis there is demyelination of the central nervous system and hence upper motor neuron signs are seen

### Multiple sclerosis: features

#### Visual

- optic neuritis: common presenting feature
- optic atrophy
- Uhthoff's phenomenon: worsening of vision following rise in body temperature
- internuclear ophthalmoplegia

#### Sensory

- pins/needles
- numbness
- trigeminal neuralgia
- Lhermitte's syndrome: paraesthesiae in limbs on neck flexion

#### Motor

- spastic weakness

#### Cerebellar

- ataxia
- tremor

#### Others

- urinary incontinence
- sexual dysfunction
- intellectual deterioration

Which of the following is least associated with Parkinsonism?

<input type="radio"/>	A. Chlorpromazine
<input type="radio"/>	B. Progressive supranuclear palsy
<input type="radio"/>	C. Dementia pugilistica
<input type="radio"/>	D. Lead poisoning
<input type="radio"/>	E. Wilson's disease

Next question

## Parkinsonism

### Causes of Parkinsonism

- Parkinson's disease
- drug-induced e.g. antipsychotics, metoclopramide - see below
- progressive supranuclear palsy
- multiple system atrophy
- Wilson's disease
- post-encephalitis
- dementia pugilistica (secondary to chronic head trauma e.g. boxing)
- toxins: carbon monoxide, MPTP

### Drugs causing Parkinsonism

- phenothiazines: e.g. chlorpromazine
- butyrophenones: haloperidol, droperidol
- metoclopramide

Domperidone does not cross the blood-brain barrier and therefore does not cause extra-pyramidal side-effects

You review a 70-year-old woman four days after she was admitted with a suspected stroke. Unfortunately she has been left with right sided sensory loss affecting her arms more than the legs and a right sided homonymous hemianopia. Functionally she has difficulty dressing her self. Examination of her cranial nerves is unremarkable. What area is the stroke most likely to have affected?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Middle cerebral artery               |
| <input type="radio"/> | B. Lacunar                              |
| <input type="radio"/> | C. Anterior cerebral artery             |
| <input type="radio"/> | D. Posterior cerebral artery            |
| <input type="radio"/> | E. Posterior inferior cerebellar artery |

[Next question](#)

## Stroke by anatomy

### Anterior cerebral artery

- contralateral hemiparesis and sensory loss, lower extremity > upper
- disconnection syndrome

### Middle cerebral artery

- contralateral hemiparesis and sensory loss, upper extremity > lower
- contralateral hemianopia
- aphasia (Wernicke's)
- gaze abnormalities

### Posterior cerebral artery

- contralateral hemianopia with macular sparing
- disconnection syndrome

### Lacunar

- present with either isolated hemiparesis, hemisensory loss or hemiparesis with limb ataxia

### Lateral medulla (posterior inferior cerebellar artery)



- ipsilateral: ataxia, nystagmus, dysphagia, facial numbness, cranial nerve palsy
- contralateral: limb sensory loss

## Pontine

- VI nerve: horizontal gaze palsy
- VII nerve
- contralateral hemiparesis

A 28-year-old woman with a history of systemic lupus erythematosus (SLE) presents with jerky, irregular movements which seem to move from one limb to another. Her symptoms are continuous and there are no other neurological features such as impairment of consciousness. Where is the neurological lesion most likely to be?

- |                       |                    |
|-----------------------|--------------------|
| <input type="radio"/> | A. Cerebellum      |
| <input type="radio"/> | B. Temporal lobe   |
| <input type="radio"/> | C. Hippocampus     |
| <input type="radio"/> | D. Thalamus        |
| <input type="radio"/> | E. Caudate nucleus |

[Next question](#)

Chorea is caused by damage to the basal ganglia, in particular the Caudate nucleus

These symptoms are consistent with chorea, which may have a number of causes including SLE. Temporal lobe epilepsy would not cause continuous symptoms.

### Chorea

Chorea describes involuntary, rapid, jerky movements which often move from one part of the body to another. Slower, sinuous movement of the limbs is termed athetosis. Chorea is caused by damage to the basal ganglia, especially the caudate nucleus.

#### Causes of chorea

- Huntington's disease, Wilson's disease, ataxic telangiectasia
- SLE, anti-phospholipid syndrome
- rheumatic fever: Sydenham's chorea
- drugs: oral contraceptive pill, L-dopa, antipsychotics
- neuroacanthocytosis
- pregnancy: chorea gravidarum
- thyrotoxicosis
- polycythaemia rubra vera
- carbon monoxide poisoning
- cerebrovascular disease

Which one of the following antibodies are associated with painful sensory neuropathy in patients with small cell lung cancer?

<input type="radio"/>	A. Anti-Ri
<input type="radio"/>	B. Anti-GAD
<input type="radio"/>	C. Anti-Ro
<input type="radio"/>	D. Anti-Hu
<input type="radio"/>	E. Anti-Yo

[Next question](#)

### Paraneoplastic syndromes affecting nervous system

#### Lambert-Eaton myasthenic syndrome

- associated with small cell lung cancer (also breast and ovarian)
- antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system
- can also occur independently as autoimmune disorder

#### Anti-Hu

- associated with small cell lung carcinoma and neuroblastomas
- sensory neuropathy - may be painful
- cerebellar syndrome
- encephalomyelitis

#### Anti-Yo

- associated with ovarian and breast cancer
- cerebellar syndrome

#### Anti-GAD antibody

- associated with breast, colorectal and small cell lung carcinoma
- stiff person's syndrome or diffuse hypertonia

#### Anti-Ri

- associated with breast and small cell lung carcinoma
- ocular opsoclonus-myoclonus

**Question 110 of 204**

Next

A 68-year-old woman presents with a two month history of electric shock like pains on the right side of her face. She describes having around 10-20 episodes a day which, each lasting for around 30-60 seconds. A recent dental check was normal. Neurological examination is unremarkable. What is the most suitable first-line management?

<input type="radio"/>	A. Amitriptyline
<input type="radio"/>	B. Sodium valproate
<input type="radio"/>	C. Carbamazepine
<input type="radio"/>	D. Atenolol
<input type="radio"/>	E. Zolmitriptan

Next question

Trigeminal neuralgia - carbamazepine is first-line

**Trigeminal neuralgia**

Trigeminal neuralgia is a pain syndrome characterised by severe unilateral pain. The vast majority of cases are idiopathic but compression of the trigeminal roots by tumours or vascular problems may occur

The International Headache Society defines trigeminal neuralgia as:

- a unilateral disorder characterised by brief electric shock-like pains, abrupt in onset and termination, limited to one or more divisions of the trigeminal nerve
- the pain is commonly evoked by light touch, including washing, shaving, smoking, talking, and brushing the teeth (trigger factors), and frequently occurs spontaneously
- small areas in the nasolabial fold or chin may be particularly susceptible to the precipitation of pain (trigger areas)
- the pains usually remit for variable periods

**Management**

- carbamazepine is first-line\*
- failure to respond to treatment or atypical features (e.g. < 50 years old) should prompt referral to neurology

\*the 2010 NICE neuropathic pain guidelines recommend using amitriptyline or pregabalin first-line for non-

diabetic neuropathic pain., but makes no specific recommendation for trigeminal neuralgia. Due to the amount of evidence supporting carbamazepine in trigeminal neuralgia and its recommendation in consensus guidelines (including Clinical Knowledge Summaries) the author does not feel that this recommendation should be changed for now

How long should a patient stop driving for following a stroke?

<input type="radio"/>	A. No restriction unless physical/visual impairment
<input type="radio"/>	B. 1 month
<input type="radio"/>	C. 3 month
<input type="radio"/>	D. 6 months
<input type="radio"/>	E. 12 months

Next question

DVLA advice post CVA: cannot drive for 1 month

### DVLA: neurological disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

#### Specific rules

- first seizure: 6 months off driving\*. For patients with established epilepsy they must be fit free for 12 months before being able to drive
- stroke or TIA: 1 month off driving
- multiple TIAs over short period of times: 3 months off driving
- craniotomy e.g. For meningioma: 1 year off driving\*\*
- pituitary tumour: craniotomy: 6 months; trans-sphenoidal surgery 'can drive when there is no debarring residual impairment likely to affect safe driving'
- narcolepsy/cataplexy: cease driving on diagnosis, can restart once 'satisfactory control of symptoms'

#### Syncope

- simple faint: no restriction
- unexplained, low risk of recurrence: 4 weeks off
- explained and treated: 4 weeks off
- unexplained: 6 months off

\*previously rule was 12 months. It is now 6 months off driving if the licence holder has undergone assessment by an appropriate specialist and no relevant abnormality has been identified on investigation, for example EEG and brain scan where indicated

\*\*if the tumour is a benign meningioma and there is no seizure history, licence can be reconsidered 6 months after surgery if remains seizure free

A 60-year-old man is diagnosed with Bell's palsy. What is the current evidenced base approach to the management of this condition?

<input type="radio"/>	A. Refer for urgent surgical decompression
<input type="radio"/>	B. Aciclovir
<input type="radio"/>	C. No treatment
<input type="radio"/>	D. Aciclovir + prednisolone
<input type="radio"/>	E. Prednisolone

[Next question](#)

### Bell's palsy

Bell's palsy may be defined as an acute, unilateral, idiopathic, facial nerve paralysis. The aetiology is unknown although the role of the herpes simplex virus has been investigated previously.

#### Features

- lower motor neuron facial nerve palsy - forehead affected\*
- patients may also notice post-auricular pain (may precede paralysis), altered taste, dry eyes, hyperacusis

#### Management

- in the past a variety of treatment options have been proposed including no treatment, prednisolone only and a combination of aciclovir and prednisolone
- following a National Institute for Health randomised controlled trial it is now recommended that prednisolone 25mg bd for 10 days should be prescribed for patients within 72 hours of onset of Bell's palsy. Adding in aciclovir gives no additional benefit
- eye care is important - prescription of artificial tears and eye lubricants should be considered

#### Prognosis

- if untreated around 15% of patients have permanent moderate to severe weakness

\*upper motor neuron lesion 'spares' upper face

Which one of the following is most associated with a good prognosis in Guillain-Barre syndrome?

<input type="radio"/>	A. Age > 40 years
<input type="radio"/>	B. Female sex
<input type="radio"/>	C. No history of a diarrhoeal illness
<input type="radio"/>	D. High anti-GM1 antibody titre
<input type="radio"/>	E. Low peak expiratory flow rate

Next question

Preceding gastrointestinal infections are associated with a poor prognosis in Guillain-Barre syndrome. The sex of the patient has not been shown to correlate with outcome

### Guillain-Barre syndrome: prognosis

Guillain-Barre syndrome (GBS) describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*)

Poor prognostic features

- age > 40 years
- poor upper extremity muscle strength
- previous history of a diarrhoeal illness (specifically *Campylobacter jejuni*)
- high anti-GM1 antibody titre
- need for ventilatory support

There is currently contradictory evidence as to whether a gradual or rapid onset of GBS is associated with a poor outcome



A 19-year-old man is diagnosed as having myoclonic seizures. What is the most appropriate first-line antiepileptic?

<input type="radio"/>	A. Sodium valproate
<input type="radio"/>	B. Carbamazepine
<input type="radio"/>	C. Topiramate
<input type="radio"/>	D. Clonazepam
<input type="radio"/>	E. Ethosuximide

[Next question](#)

### Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Generalised tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures\* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

## Partial seizures

- carbamazepine
- second line: lamotrigine\*\*, sodium valproate

\*carbamazepine may actually exacerbate absence seizure

\*\*the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

A 27-year-old woman is reviewed due to sudden loss of vision in her left eye. She is known to have severe rheumatoid arthritis and is treated currently with methotrexate, infliximab and prednisolone. She has in the past also used sulfasalazine and hydroxychloroquine. For the past 6 weeks she has developed troublesome headaches. Examination demonstrates bilateral papilloedema. Which one of the following is most likely to be responsible for this presentation?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Chloroquine retinopathy    |
| <input type="radio"/> | B. Prednisolone               |
| <input type="radio"/> | C. Infliximab                 |
| <input type="radio"/> | D. Methotrexate               |
| <input type="radio"/> | E. Keratoconjunctivitis sicca |

[Next question](#)

This patient has developed intracranial hypertension probably secondary to prednisolone. Patients may lose sight suddenly if the optic nerve becomes compressed

### Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (also known as pseudotumour cerebri and formerly benign intracranial hypertension) is a condition classically seen in young, overweight females.

#### Features

- headache
- blurred vision
- papilloedema (usually present)
- enlarged blind spot
- sixth nerve palsy may be present

#### Risk factors

- obesity
- female sex
- pregnancy
- drugs\*: oral contraceptive pill, steroids, tetracycline, vitamin A

#### Management

- weight loss
- diuretics e.g. acetazolamide
- repeated lumbar puncture

- surgery: optic nerve sheath decompression and fenestration may be needed to prevent damage to the optic nerve. A lumboperitoneal or ventriculoperitoneal shunt may also be performed to reduce intracranial pressure

\*if intracranial hypertension is thought to occur secondary to a known causes (e.g. Medication) then it is of course not idiopathic

A man is recovering after having an operation to remove a meningioma in his left temporal lobe. What sort of visual field defect is he at risk of having following the procedure?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Right inferior homonymous quadrantanopia        |
| <input type="radio"/> | B. Right superior homonymous quadrantanopia        |
| <input type="radio"/> | C. Left inferior homonymous quadrantanopia         |
| <input type="radio"/> | D. Right homonymous hemianopia with macula sparing |
| <input type="radio"/> | E. Left superior homonymous quadrantanopia         |

[Next question](#)

Visual field defects:

- left homonymous hemianopia means visual field defect to the left, i.e. lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

### Visual field defects

The main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

A congruous defect simply means complete or symmetrical visual field loss and conversely an incongruous defect is incomplete or asymmetric. Please see the link for an excellent diagram.

Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias\*

- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe

- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

#### Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

\*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details:

<http://www.ncbi.nlm.nih.gov/pubmed/9109741>

A 63-year-old man is prescribed selegiline for Parkinson's disease. What is the mechanism of action?

<input type="radio"/>	A. Dopamine receptor antagonist
<input type="radio"/>	B. Dopamine receptor agonist
<input type="radio"/>	C. Monoamine Oxidase-B inhibitor
<input type="radio"/>	D. Antimuscarinic
<input type="radio"/>	E. Catechol-O-Methyl Transferase inhibitor

Next question

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

## Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

## COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

## Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benzotropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction



Which one of the following is most associated with downbeat nystagmus?

<input type="radio"/>	A. Arnold-Chiari malformation
<input type="radio"/>	B. Pseudobulbar palsy
<input type="radio"/>	C. Jugular foramen syndrome
<input type="radio"/>	D. Acoustic neuroma
<input type="radio"/>	E. Cerebellar vermis lesions

Next question

## Nystagmus

Upbeat nystagmus

- cerebellar vermis lesions

Downbeat nystagmus - foramen magnum lesions

- Arnold-Chiari malformation

Which one of the following is least associated with ptosis?

<input type="radio"/>	A. Horner's syndrome
<input type="radio"/>	B. Myotonic dystrophy
<input type="radio"/>	C. Lambert-Eaton syndrome
<input type="radio"/>	D. Third nerve palsy
<input type="radio"/>	E. Motor neuron disease

Next question

## Ptosis

Ptosis may be unilateral or bilateral

Causes of bilateral ptosis:

- myotonic dystrophy
- myasthenia gravis\*
- syphilis
- congenital

Causes of unilateral ptosis, as above plus:

- third nerve palsy
- Horner's

\*ptosis is much less common in Lambert-Eaton syndrome than myasthenia gravis

A 31-year-old female with progressive leg weakness has nerve conduction studies for suspected Guillain-Barre syndrome. Which one of the following findings would be most consistent with this diagnosis?

<input type="radio"/>	A. Reduced conduction velocity
<input type="radio"/>	B. Extended series of repetitive discharges lasting up to 30 seconds
<input type="radio"/>	C. Increased conduction velocity
<input type="radio"/>	D. Diminished response to repetitive stimulation
<input type="radio"/>	E. Reduced wave amplitude

[Next question](#)

Slowing of the nerve conduction velocity usually indicates there is damage to the myelin sheath, as in Guillain-Barre syndrome

### Nerve conduction studies

Nerve conduction studies (NCS) are useful in determining between axonal and demyelinating pathology

#### Axonal

- normal conduction velocity
- reduced amplitude

#### Demyelinating

- reduced conduction velocity
- normal amplitude

A 34-year-old woman who presents with confusion, headache and fever is admitted to the Emergency Department. Shortly after admission she has a seizure. A MRI scan is performed which shows patchy haemorrhagic changes in the temporal lobe. Given the likely diagnosis, what is the treatment of choice?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Supportive treatment + intravenous cefotaxime     |
| <input type="radio"/> | B. Supportive treatment + intravenous aciclovir      |
| <input type="radio"/> | C. Supportive treatment + intravenous amphotericin B |
| <input type="radio"/> | D. Supportive treatment alone                        |
| <input type="radio"/> | E. Supportive treatment + intravenous immunoglobulin |

[Next question](#)

### Herpes simplex encephalitis

Herpes simplex (HSV) encephalitis is a common topic in the exam. The virus characteristically affects the temporal lobes - questions may give the result of imaging or describe temporal lobe signs e.g. aphasia

#### Features

- fever, headache, psychiatric symptoms, seizures, vomiting
- focal features e.g. aphasia
- peripheral lesions (e.g. cold sores) have no relation to presence of HSV encephalitis

#### Pathophysiology

- HSV-1 responsible for 95% of cases in adults
- typically affects temporal and inferior frontal lobes

#### Investigation

- CSF: lymphocytosis, elevated protein
- PCR for HSV
- CT: medial temporal and inferior frontal changes (e.g. petechial haemorrhages) - normal in one-third of patients
- MRI is better
- EEG pattern: lateralised periodic discharges at 2 Hz

#### Treatment

- intravenous aciclovir

The prognosis is dependent on whether aciclovir is commenced early. If treatment is started promptly the mortality is 10-20%. Left untreated the mortality approaches 80%

A 52-year-old man is reviewed in the neurology clinic. He has been referred due to the development of difficulty in finding the right words whilst speaking. His comprehension of normal conversation has however remained normal. Where is the likely lesion?

<input type="radio"/>	A. Anterior temporal lobe
<input type="radio"/>	B. Posterior temporal lobe
<input type="radio"/>	C. Parietal lobe
<input checked="" type="radio"/>	D. Posterior frontal lobe
<input type="radio"/>	E. Anterior frontal lobe

[Next question](#)

This man has expressive aphasia due to a lesion in Broca's area, located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus

## Brain lesions

The following neurological disorders/features may allow localisation of a brain lesion:

### Gross anatomy

#### Parietal lobe lesions

- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

#### Occipital lobe lesions

- homonymous hemianopia (with macula sparing)
- cortical blindness
- visual agnosia

#### Temporal lobe lesion

- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia
- prosopagnosia (difficulty recognising faces)

## Frontal lobes lesions

- expressive (Broca's) aphasia: located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus
- disinhibition
- perseveration
- anosmia
- inability to generate a list

## Cerebellum lesions

- midline lesions: gait and truncal ataxia
- hemisphere lesions: intention tremor, past pointing, dysdiadokinesis, nystagmus

## More specific areas

Medial thalamus and mammillary bodies of the hypothalamus	Wernicke and Korsakoff syndrome
Subthalamic nucleus of the basal ganglia	Hemiballism
Striatum (caudate nucleus) of the basal ganglia	Huntington chorea
Substantia nigra of the basal ganglia	Parkinson's disease
Amygdala	KluverBucy syndrome (hypersexuality, hyperorality, hyperphagia, visual agnosia)

A 34-year-old accountant presents with a one week history of pain around his right eye occurring once or twice a day. They are described as being very severe and lasting between 10-30 minutes each. He also describes a feeling of a blocked nose. What is the treatment of choice to treat this current episode?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Ibuprofen                           |
| <input type="radio"/> | B. Acetazolamide + topical pilocarpine |
| <input type="radio"/> | C. Prednisolone                        |
| <input type="radio"/> | D. Subcutaneous sumatriptan            |
| <input type="radio"/> | E. Ergotamine                          |

Next question

Cluster headache - acute treatment: subcutaneous sumatriptan + 100% O<sub>2</sub>

Standard analgesia is rarely effective in cluster headaches. 100% oxygen may also be used

### Cluster headache

Cluster headaches\* are more common in men (5:1) and smokers

#### Features

- pain typical occurs once or twice a day, each episode lasting 15 mins - 2 hours
- clusters typically last 4-12 weeks
- intense pain around one eye (recurrent attacks 'always' affect same side)
- patient is restless during an attack
- accompanied by redness, lacrimation, lid swelling
- nasal stuffiness
- miosis and ptosis in a minority

#### Management

- acute: 100% oxygen, subcutaneous sumatriptan, nasal lidocaine
- prophylaxis: verapamil, prednisolone
- consider specialist referral

\*some neurologists use the term trigeminal autonomic cephalgia to group a number of conditions including cluster headache, paroxysmal hemicrania and short-lived unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). It is recommended such patients are referred for specialist assessment as specific treatment may be required, for example it is known paroxysmal hemicrania responds very well to indomethacin

A 75-year-old man is seen with his family who are concerned about his memory and behaviour over the past six months. A cognitive assessment is performed which seems to confirm the family's concerns. A series of blood tests are performed to exclude reversible causes. A full blood count, urea and electrolytes, liver function tests and bone profile are requested. Which other blood tests is it most appropriate to request?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Thyroid function tests, vitamin B12, glucose, syphilis, HIV    |
| <input type="radio"/> | B. Thyroid function tests, vitamin B12, folate, glucose           |
| <input type="radio"/> | C. Thyroid function tests, vitamin B12, folate, glucose, syphilis |
| <input type="radio"/> | D. Thyroid function tests, vitamin B12                            |
| <input type="radio"/> | E. Thyroid function tests, vitamin B12, syphilis, HIV             |

[Next question](#)

NICE do not recommend routine testing for syphilis and HIV.

## Dementia

Dementia is thought to affect over 700,000 people in the UK and accounts for a large amount of health and social care spending. The most common cause of dementia in the UK is Alzheimer's disease followed by vascular and Lewy body dementia. These conditions may coexist.

### Features

- diagnosis can be difficult and is often delayed
- the mini-mental state examination is widely used. A score of 24 or less out of 30 suggests dementia

### Management

- in primary care a blood screen is usually sent to exclude reversible causes (e.g. Hypothyroidism). NICE recommend the following tests: FBC, U&E, LFTs, calcium, glucose, TFTs, vitamin B12 and folate levels. Patients are now commonly referred on to old-age psychiatrists (sometimes working in 'memory clinics').
- in secondary care neuroimaging is performed\* to exclude other reversible conditions (e.g. Subdural haematoma, normal pressure hydrocephalus) and help provide information on aetiology to guide prognosis and management

\*in the 2011 NICE guidelines structural imaging was said to be essential in the investigation of dementia



A 54-year-old man presents with a persistent tremor. On examination there is 6-8 Hz tremor of the arms which is worse when his arms are outstretched. His father suffered from a similar complaint. What is the most suitable first-line treatment?

<input type="radio"/>	A. Amitriptyline
<input type="radio"/>	B. Propranolol
<input type="radio"/>	C. D-penicillamine
<input type="radio"/>	D. Levodopa
<input type="radio"/>	E. Diazepam

Next question

Essential tremor is an AD condition that is made worse when arms are outstretched, made better by alcohol and propranolol

This patient has a typical history of essential tremor. Propranolol is generally considered the first-line treatment

### Essential tremor

Essential tremor (previously called benign essential tremor) is an autosomal dominant condition which usually affects both upper limbs

#### Features

- postural tremor: worse if arms outstretched
- improved by alcohol and rest
- most common cause of titubation (head tremor)

#### Management

- propranolol is first-line
- primidone is sometimes used

A 49-year-old man presents to the Emergency Department complaining of visual disturbance. Examination reveals a right incongruous homonymous hemianopia. Where is the lesion most likely to be?

<input type="radio"/>	A. Left optic tract
<input type="radio"/>	B. Left optic radiation
<input type="radio"/>	C. Right optic tract
<input type="radio"/>	D. Right optic radiation
<input type="radio"/>	E. Optic chiasm

[Next question](#)

### Visual field defects

The main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

A congruous defect simply means complete or symmetrical visual field loss and conversely an incongruous defect is incomplete or asymmetric. Please see the link for an excellent diagram.

#### Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

#### Homonymous quadrantanopias\*

- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe
- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

#### Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour

- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

\*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details:

<http://www.ncbi.nlm.nih.gov/pubmed/9109741>

Each one of the following is associated with Friedreich's ataxia, except:

<input type="radio"/>	A. Increased risk of deep vein thrombosis
<input type="radio"/>	B. Optic atrophy
<input type="radio"/>	C. Cardiomyopathy
<input type="radio"/>	D. Nystagmus
<input type="radio"/>	E. High-arched palate

Next question

### Friedreich's ataxia

Friedreich's ataxia is the most common of the early-onset hereditary ataxias. It is an autosomal recessive, trinucleotide repeat disorder characterised by a GAA repeat in the X25 gene on chromosome 9 (frataxin). Friedreich's ataxia is unusual amongst trinucleotide repeat disorders in not demonstrating the phenomenon of anticipation

The typical age of onset is 10-15 years old. Gait ataxia is the most common presenting feature.

#### Neurological features

- absent ankle jerks/extensor plantars
- cerebellar ataxia
- optic atrophy
- spinocerebellar tract degeneration

#### Other features

- hypertrophic obstructive cardiomyopathy (90%, most common cause of death)
- diabetes mellitus (10-20%)
- high-arched palate

A 61-year-old woman presents with bilateral tinnitus. She reports no change in her hearing or other ear-related symptoms. Ear and cranial nerve examination is unremarkable. Which medication is she most likely to have recently started?

- ☐ A. Ciprofloxacin
- ☐ B. Nifedipine
- ☐ C. Repaglinide
- ☐ D. Quinine
- ☐ E. Bendroflumethiazide

[Next question](#)

## Tinnitus

Causes of tinnitus include:

<b>Meniere's disease</b>	Associated with hearing loss, vertigo, tinnitus and sensation of fullness or pressure in one or both ears
<b>Otosclerosis</b>	Onset is usually at 20-40 years Conductive deafness Tinnitus Normal tympanic membrane* Positive family history
<b>Acoustic neuroma</b>	Hearing loss, vertigo, tinnitus Absent corneal reflex is important sign Associated with neurofibromatosis type 2
<b>Hearing loss</b>	Causes include excessive loud noise and presbycusis
<b>Drugs</b>	Aspirin Aminoglycosides Loop diuretics Quinine

Other causes include

- impacted ear wax
- chronic suppurative otitis media

\*10% of patients may have a 'flamingo tinge', caused by hyperaemia

What is the most common clinical pattern seen in motor neuron disease?

<input type="radio"/>	A. Progressive muscular atrophy
<input type="radio"/>	B. Progressive bulbar palsy
<input type="radio"/>	C. Spinocerebellar ataxia
<input type="radio"/>	D. Relapsing-remitting
<input type="radio"/>	E. Amyotrophic lateral sclerosis

Next question

### Motor neuron disease: types

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, primary lateral sclerosis, progressive muscular atrophy and progressive bulbar palsy. In some patients however, there is a combination of clinical patterns

Amyotrophic lateral sclerosis (50% of patients)

- typically LMN signs in arms and UMN signs in legs
- in familial cases the gene responsible lies on chromosome 21 and codes for superoxide dismutase

Primary lateral sclerosis

- UMN signs only

Progressive muscular atrophy

- LMN signs only
- affects distal muscles before proximal
- carries best prognosis

Progressive bulbar palsy

- palsy of the tongue, muscles of chewing/swallowing and facial muscles due to loss of function of brainstem motor nuclei
- carries worst prognosis

Each one of the following is associated with ataxic telangiectasia, except:

<input type="radio"/>	A. Telangiectasia
<input type="radio"/>	B. Cerebellar ataxia
<input type="radio"/>	C. Autosomal dominant inheritance
<input type="radio"/>	D. Recurrent chest infections
<input type="radio"/>	E. Increased risk of malignancy

Next question

## Ataxic telangiectasia

### Basics

- autosomal recessive disorder
- combined immunodeficiency disorder

### Features

- cerebellar ataxia
- telangiectasia
- recurrent chest infections
- 10% risk of developing malignancy, lymphoma or leukaemia, but also non-lymphoid tumours

During a routine cranial nerve examination the following findings are observed:

Rinne's test:	Air conduction > bone conduction in both ears
Weber's test:	Localises to the right side

What do these tests imply?

- ☐ A. Left conductive deafness
- ☐ B. Normal hearing
- ☐ C. Right conductive deafness
- ☐ D. Right sensorineural deafness
- ☐ E. Left sensorineural deafness

Next question

In Weber's test if there is a sensorineural problem the sound is localised to the unaffected side (right) indicating a problem on the left side

### Rinne's and Weber's test

Performing both Rinne's and Weber's test allows differentiation of conductive and sensorineural deafness.

#### Rinne's test

- tuning fork is placed over the mastoid process until the sound is no longer heard, followed by repositioning just over external acoustic meatus
- air conduction (AC) is normally better than bone conduction (BC)
- if BC > AC then conductive deafness

#### Weber's test

- tuning fork is placed in the middle of the forehead equidistant from the patient's ears
- the patient is then asked which side is loudest
- in unilateral sensorineural deafness, sound is localised to the unaffected side
- in unilateral conductive deafness, sound is localised to the affected side



A 40-year-old man undergoes a temporal lobectomy after the discovery of a brain tumour. Which one of the following consequences would be least likely to develop?

<input type="radio"/>	A. Prosopagnosia
<input type="radio"/>	B. Astereognosis
<input type="radio"/>	C. Wernicke's aphasia
<input type="radio"/>	D. Superior homonymous quadrantanopia
<input type="radio"/>	E. Auditory agnosia

[Next question](#)

## Brain lesions

The following neurological disorders/features may allow localisation of a brain lesion:

### Gross anatomy

#### Parietal lobe lesions

- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

#### Occipital lobe lesions

- homonymous hemianopia (with macula sparing)
- cortical blindness
- visual agnosia

#### Temporal lobe lesion

- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia
- prosopagnosia (difficulty recognising faces)

## Frontal lobes lesions

- expressive (Broca's) aphasia: located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus
- disinhibition
- perseveration
- anosmia
- inability to generate a list

## Cerebellum lesions

- midline lesions: gait and truncal ataxia
- hemisphere lesions: intention tremor, past pointing, dysdiadokinesis, nystagmus

## More specific areas

Medial thalamus and mammillary bodies of the hypothalamus	Wernicke and Korsakoff syndrome
Subthalamic nucleus of the basal ganglia	Hemiballism
Striatum (caudate nucleus) of the basal ganglia	Huntington chorea
Substantia nigra of the basal ganglia	Parkinson's disease
Amygdala	KluverBucy syndrome (hypersexuality, hyperorality, hyperphagia, visual agnosia)

Which one of the following is least associated with the development of chorea?

<input type="radio"/>	A. Ataxic telangiectasia
<input type="radio"/>	B. SLE
<input type="radio"/>	C. Wilson's disease
<input type="radio"/>	D. Pregnancy
<input type="radio"/>	E. Infective endocarditis

Next question

Chorea can be a very rare manifestation of infective endocarditis, following embolisation to the basal ganglia. It is however the least likely of the above five options

### Chorea

Chorea describes involuntary, rapid, jerky movements which often move from one part of the body to another. Slower, sinuous movement of the limbs is termed athetosis. Chorea is caused by damage to the basal ganglia, especially the caudate nucleus.

#### Causes of chorea

- Huntington's disease, Wilson's disease, ataxic telangiectasia
- SLE, anti-phospholipid syndrome
- rheumatic fever: Sydenham's chorea
- drugs: oral contraceptive pill, L-dopa, antipsychotics
- neuroacanthocytosis
- pregnancy: chorea gravidarum
- thyrotoxicosis
- polycythaemia rubra vera
- carbon monoxide poisoning
- cerebrovascular disease

A 43-year-old woman with multiple sclerosis presents for review. She is having increasing problems with painful involuntary contractions of the leg muscles. What is the most appropriate first-line therapy?

<input type="radio"/>	A. Referral for relaxation therapy
<input type="radio"/>	B. Baclofen
<input type="radio"/>	C. Diazepam
<input type="radio"/>	D. Dantrolene
<input type="radio"/>	E. Natalizumab

[Next question](#)

### Multiple sclerosis: management

Treatment in multiple sclerosis is focused at reducing the frequency and duration of relapses. There is no cure. High dose steroids (e.g. IV methylprednisolone) may be given for 3-5 days to shorten the length of an acute relapse. Baclofen is helpful in controlling spasticity. Hallucinations are occasionally seen on the withdrawal of baclofen

Beta-interferon has been shown to reduce the relapse rate by up to 30%. Certain criteria have to be met before it is used:

- relapsing-remitting disease + 2 relapses in past 2 years + able to walk 100m unaided
- secondary progressive disease + 2 relapses in past 2 years + able to walk 10m (aided or unaided)
- reduces number of relapses and MRI changes, however doesn't reduce overall disability

Other drugs used in the management of multiple sclerosis include:

- glatiramer acetate: immunomodulating drug
- natalizumab: a recombinant monoclonal antibody that antagonises Alpha4Beta1-integrin found on the surface of leucocytes, thus inhibiting migration of leucocytes across the endothelium into parenchymal tissue

### Symptom control

- spasticity: baclofen and gabapentin are first-line. Other options include diazepam, dantrolene and tizanidine

**Question 135 of 204**

Next

A 19-year-old man presents with a two-day history of a diffuse headache and sore throat. He is pyrexial at 37.8°C and is reluctant to have a fundoscopy due to photophobia. A lumbar puncture is performed:

Serum glucose	5.9 mmol/l
---------------	------------

Lumbar puncture reveals:

Appearance	Clear
Glucose	4.1 mmol/l
Protein	0.3 g/l
White cells	lymphocytes 2 /mm <sup>3</sup> polymorphs 0 /mm <sup>3</sup>

What is the most likely diagnosis?

<input type="radio"/>	A. Guillain-Barre syndrome
<input type="radio"/>	B. Viral meningitis
<input type="radio"/>	C. Bacterial meningitis
<input type="radio"/>	D. Cerebral malaria
<input type="radio"/>	E. Normal CSF result

Next question

There results are consistent with normal CSF - an alternative diagnosis should be considered

**Meningitis: CSF analysis**

The table below summarises the characteristic cerebrospinal fluid (CSF) findings in meningitis:

	<b>Bacterial</b>	<b>Viral</b>	<b>Tuberculous</b>
<b>Appearance</b>	Cloudy	Clear/cloudy	Fibrin web
<b>Glucose</b>	Low (< 1/2 plasma)	Normal*	Low (< 1/2 plasma)
<b>Protein</b>	High (> 1 g/l)	Normal/raised	High (> 1 g/l)
<b>White cells</b>	10 - 5,000 polymorphs/mm <sup>3</sup>	15 - 1,000 lymphocytes/mm <sup>3</sup>	10 - 1,000 lymphocytes/mm <sup>3</sup>

The Ziehl-Neelsen stain is only 20% sensitive in the detection of tuberculous meningitis and therefore PCR is sometimes used (sensitivity = 75%)

\*mumps is unusual in being associated with a low glucose level in a proportion of cases. A low glucose may also be seen in herpes encephalitis

Serum glucose	4.9 mmol/l
---------------	------------

**Lumbar puncture reveals:**

Opening pressure	14 cmCSF
Appearance	Cloudy
Glucose	1.7 mmol/l
Protein	1.9 g/l
White cells	900 / mm <sup>3</sup> (90% polymorphs)

An 84-year-old female is admitted for a urinary tract infection. On the second night of admission she is found wandering outside the ward in an agitated state. Despite appropriate antibiotic therapy, nursing care and modification of her environment she remains agitated and aggressive and it is judged a potential danger to herself. What is the most appropriate management?

<input type="radio"/>	A. Haloperidol 5 mg orally
<input type="radio"/>	B. Lorazepam 2 mg intramuscularly
<input type="radio"/>	C. Haloperidol 0.5 mg orally
<input type="radio"/>	D. Lorazepam 0.5 mg orally
<input type="radio"/>	E. Ask for on-call psychiatric opinion for consideration of section under the Mental Health Act

[Next question](#)

Whilst many doctors may use oral lorazepam in this situation the Royal College of Physicians recommend haloperidol as the first-line sedative. NICE also advocate the use of olanzapine.

### Acute confusional state

Acute confusional state is also known as delirium or acute organic brain syndrome. It affects up to 30% of elderly patients admitted to hospital.

Features - wide variety of presentations

- memory disturbances (loss of short term > long term)
- may be very agitated or withdrawn
- disorientation
- mood change
- visual hallucinations
- disturbed sleep cycle
- poor attention

### Management

- treatment of underlying cause
- modification of environment
- the 2006 Royal College of Physicians publication 'The prevention, diagnosis and management of delirium in older people: concise guidelines' recommended haloperidol 0.5 mg as the first-line sedative
- the 2010 NICE delirium guidelines advocate the use of haloperidol or olanzapine

Which one of the following causes of Horner's syndrome is due to a lesion in the post-ganglionic part of the nerve supply?

<input type="radio"/>	A. Internal carotid aneurysm
<input type="radio"/>	B. Stroke
<input type="radio"/>	C. Syringomyelia
<input type="radio"/>	D. Pancoast's tumour
<input type="radio"/>	E. Thyroidectomy

[Next question](#)

Horner's syndrome - anhydrosis determines site of lesion:

- head, arm, trunk = central lesion: stroke, syringomyelia
- just face = pre-ganglionic lesion: Pancoast's, cervical rib
- absent = post-ganglionic lesion: carotid artery

## Horner's syndrome

### Features

- miosis (small pupil)
- ptosis
- enophthalmos\* (sunken eye)
- anhydrosis (loss of sweating one side)

### Distinguishing between causes

- heterochromia (difference in iris colour) is seen in congenital Horner's
- anhydrosis: see below

Central lesions	Pre-ganglionic lesions	Post-ganglionic lesions
Anhydrosis of the face, arm and trunk	Anhydrosis of the face	No anhydrosis
Stroke Syringomyelia Multiple sclerosis Tumour Encephalitis	Pancoast's tumour Thyroidectomy Trauma Cervical rib	Carotid artery dissection Carotid aneurysm Cavernous sinus thrombosis Cluster headache

\*in reality the appearance is due to a narrow palpebral aperture rather than true enophthalmos



A 31-year-old man presents around four weeks after a non-specific viral illness characterised by fever, lethargy and sore throat. For the past week he has noticed increasing weakness in his legs which has now started to extend to his arms. On examination he has reduced power, reflexes and slightly reduced sensation in his lower limbs. A few days after admission he becomes short-of-breath. His forced vital capacity (FVC) starts to fall and he is transferred to ITU. Given the likely diagnosis, what is the treatment of choice

- |                                  |                                |
|----------------------------------|--------------------------------|
| <input type="radio"/>            | A. Neostigmine                 |
| <input type="radio"/>            | B. Intravenous corticosteroids |
| <input type="radio"/>            | C. Haemofiltration             |
| <input checked="" type="radio"/> | D. Intravenous immunoglobulin  |
| <input type="radio"/>            | E. Riluzole                    |

[Next question](#)

This patient has developed Guillain-Barre syndrome (GBS) secondary to a viral illness, possibly the Epstein-Barr virus. The ascending weakness and areflexia point to a diagnosis of GBS.

#### Guillain-Barre syndrome: management

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*).

##### Management

- plasma exchange
- IV immunoglobulins (IVIG): as effective as plasma exchange. No benefit in combining both treatments. IVIG may be easier to administer and tends to have fewer side-effects
- steroids and immunosuppressants have not been shown to be beneficial
- FVC regularly to monitor respiratory function

##### Prognosis

- 20% suffer permanent disability, 5% die

A 72-year-old woman with a past history of treated hypertension presents to the Emergency Department. Yesterday she had a 2 hour episode where she couldn't find the right word when speaking. This has never happened before and there were no associated features. Neurological examination is unremarkable and blood pressure was 150/100 mmHg. Her only current medication is amlodipine. What is the most appropriate management?

- ☐ A. Aspirin 300mg immediately + specialist review within 2 weeks
- ☐ B. Specialist review within 2 weeks
- ☐ C. Aspirin 300mg immediately + specialist review within 24 hours
- ☐ D. Aspirin 75mg + outpatient CT brain
- ☐ E. Specialist review within 24 hours

[Next question](#)

This patient's age, blood pressure and duration of symptoms would put her in a higher risk category. Current guidelines advocate specialist review within 24 hours

### Transient ischaemic attack

NICE issued updated guidelines relating to stroke and transient ischaemic attack (TIA) in 2008. They advocated the use of the ABCD2 prognostic score for risk stratifying patients who've had a suspected TIA:

	Criteria	Points
<b>A</b>	Age $\geq$ 60 years	1
<b>B</b>	Blood pressure $\geq$ 140/90 mmHg	1
<b>C</b>	Clinical features	
	- Unilateral weakness	2
	- Speech disturbance, no weakness	1
<b>D</b>	Duration of symptoms	
	- > 60 minutes	2
	- 10-59 minutes	1
	Patient has diabetes	1

This gives a total score ranging from 0 to 7. People who have had a suspected TIA who are at a higher risk of stroke (that is, with an ABCD2 score of 4 or above) should have:

- aspirin (300 mg daily) started immediately
- specialist assessment and investigation within 24 hours of onset of symptoms
- measures for secondary prevention introduced as soon as the diagnosis is confirmed, including discussion of individual risk factors

If the ABCD2 risk score is 3 or below:

- specialist assessment within 1 week of symptom onset, including decision

on brain imaging

- if vascular territory or pathology is uncertain, refer for brain imaging

People with crescendo TIAs (two or more episodes in a week) should be treated as being at high risk of stroke, even though they may have an ABCD2 score of 3 or below.

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- aspirin plus modified-release (MR) dipyridamole is still recommended as first choice for people who have had a TIA, but now there is no recommended limit on the duration of treatment. Clopidogrel is not recommended
- MR dipyridamole monotherapy is recommended after TIA only if aspirin is contraindicated or not tolerated, again with no limit on duration of treatment.

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST\* criteria or > 50% according to NASCET\*\* criteria

\*European Carotid Surgery Trialists' Collaborative Group

\*\*North American Symptomatic Carotid Endarterectomy Trial

The following drugs commonly exacerbate myasthenia gravis, except:

<input type="radio"/>	A. Methotrexate
<input type="radio"/>	B. Gentamicin
<input type="radio"/>	C. Beta-blockers
<input type="radio"/>	D. Quinidine
<input type="radio"/>	E. Penicillamine

Next question

### Myasthenia gravis: exacerbating factors

The most common exacerbating factor is exertion resulting in fatigability, which is the hallmark feature of myasthenia gravis . Symptoms become more marked during the day

The following drugs may exacerbate myasthenia:

- penicillamine
- quinidine, procainamide
- beta-blockers
- lithium
- phenytoin
- gentamicin

A 62-year-old man is admitted to the Emergency Department with a left hemiplegia. His symptoms started around 5 hours but he initially thought he had slept in an awkward position. He has no past medical history of note but on examination is found to have an irregular pulse of 150 / min. The ECG confirms atrial fibrillation. A CT head is immediately arranged and reported as normal. What is the most appropriate initial management?

- ☐ A. Aspirin
- ☐ B. Aspirin + dipyridamole
- ☐ C. Alteplase
- ☐ D. Warfarin
- ☐ E. Aspirin + warfarin

Next question

Rate control should also be initiated. He is outside the thrombolysis window so alteplase is not an option. The 2004 RCP guidelines recommend that anticoagulation should be commenced 14 days after an ischaemic stroke. Earlier anticoagulation may exacerbate any secondary haemorrhage.

Dipyridamole should not be used in the acute phase.

### Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued stroke guidelines in 2008, although they modified their guidance with respect to antiplatelet therapy in 2010.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy\*
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commenced on a statin. Many physicians will delay treatment until after at least 48 hours due to the risk of haemorrhagic transformation

### Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 hours\*\* of onset of stroke symptoms (unless as part of a clinical trial)

- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

## **Secondary prevention**

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- clopidogrel is now recommended by NICE ahead of combination use of aspirin plus modified release (MR) dipyridamole in people who have had an ischaemic stroke
- aspirin plus MR dipyridamole is now recommended after an ischaemic stroke only if clopidogrel is contraindicated or not tolerated, but treatment is no longer limited to 2 years' duration
- MR dipyridamole alone is recommended after an ischaemic stroke only if aspirin or clopidogrel are contraindicated or not tolerated, again with no limit on duration of treatment

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST\*\*\* criteria or > 50% according to NASCET\*\*\*\* criteria

\*the 2009 Controlling hypertension and hypotension immediately post-stroke (CHHIPS) trial may change thinking on this but guidelines have yet to change to reflect this

\*\*SIGN recommend a window of 4.5 hours

\*\*\*European Carotid Surgery Trialists' Collaborative Group

\*\*\*\*North American Symptomatic Carotid Endarterectomy Trial

A 27-year-old female presents complaining of generalised weakness. Examination of her face reveals bilateral ptosis, dysarthric speech and a slow-relaxing grip. What is the most likely diagnosis?

- ☐ A. Myotonic dystrophy
- ☐ B. Myasthenia gravis
- ☐ C. Multiple sclerosis
- ☐ D. Ataxic telangiectasia
- ☐ E. Friedreich's ataxia

[Next question](#)

### Dystrophia myotonica - DM1

- distal weakness initially
- autosomal dominant
- diabetes
- dysarthria

The slow-relaxing grip may be noticed on initial hand-shake with the patient and is typical of myotonic dystrophy. Dysarthric speech is secondary to myotonia of the tongue and pharynx

### Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

#### Genetics

- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	DM2
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent

	- Severe congenital form not seen
--	-----------------------------------

### General features

- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

### Other features

- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia



A 63-year-old woman with motor neuron disease is reviewed in clinic. Which one of the following interventions will have the greatest effect on survival?

<input type="radio"/>	A. Regular chest physiotherapy
<input type="radio"/>	B. Total parental nutrition
<input type="radio"/>	C. Riluzole
<input type="radio"/>	D. Antioxidant supplementation
<input type="radio"/>	E. Non-invasive ventilation

[Next question](#)

Motor neuron disease - treatment: NIV is better than riluzole

### Motor neuron disease: management

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy

#### Riluzole

- anti-glutamate drug
- used mainly in amyotrophic lateral sclerosis
- prolongs life by about 3 months
- expensive

#### Respiratory care

- non-invasive ventilation (usually BIPAP) is used at night
- studies have shown a survival benefit of around 7 months

#### Prognosis

- poor: 50% of patients die within 3 years

A 70-year-old man is investigated for involuntary, jerking movements of his arms. His symptoms seem to resolve when he is asleep. Damage to which one of the following structures may lead to hemiballism?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Substantia nigra    |
| <input type="radio"/> | B. Red nucleus         |
| <input type="radio"/> | C. Subthalamic nucleus |
| <input type="radio"/> | D. Globus pallidus     |
| <input type="radio"/> | E. Frontal lobe        |

[Next question](#)

Hemiballism is caused by damage to the subthalamic nucleus

### Hemiballism

Hemiballism occurs following damage to the subthalamic nucleus. Ballistic movements are involuntary, sudden, jerking movements which occur contralateral to the side of the lesion. The ballistic movements primarily affect the proximal limb musculature whilst the distal muscles may display more choreiform-like movements

Symptoms may decrease whilst the patient is asleep.

Antidopaminergic agents (e.g. Haloperidol) are the mainstay of treatment

A 63-year-old man is diagnosed as having restless legs syndrome. What is the most relevant blood test to perform?

<input type="radio"/>	A. ESR
<input type="radio"/>	B. Ferritin
<input type="radio"/>	C. Blood glucose
<input type="radio"/>	D. Urea and electrolytes
<input type="radio"/>	E. Liver function tests

A case could be made for all the above tests but a low serum ferritin is most likely to be a cause of secondary restless legs syndrome

### Restless legs syndrome

Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. It is extremely common, affecting between 2-10% of the general population. Males and females are equally affected and a family history may be present

#### Clinical features

- uncontrollable urge to move legs (akathisia). Symptoms initially occur at night but as condition progresses may occur during the day. Symptoms are worse at rest
- paraesthesias e.g. 'crawling' or 'throbbing' sensations
- movements during sleep may be noted by the partner - periodic limb movements of sleep (PLMS)

#### Causes and associations

- there is a positive family history in 50% of patients with idiopathic RLS
- iron deficiency anaemia
- uraemia
- diabetes mellitus
- pregnancy

The diagnosis is clinical although bloods to exclude iron deficiency anaemia may be appropriate

#### Management

- simple measures: walking, stretching, massaging affected limbs
- treat any iron deficiency
- dopamine agonists are first-line treatment (e.g. Pramipexole, ropinirole)
- benzodiazepines
- gabapentin

You are reviewing a patient with Parkinson's disease. Which one of the following types of medications has been most linked with impulse control disorders?

<input type="radio"/>	A. Levodopa
<input type="radio"/>	B. Catechol-O-Methyl Transferase inhibitors
<input type="radio"/>	C. Dopamine receptor agonists
<input type="radio"/>	D. Amantadine
<input type="radio"/>	E. Monoamine Oxidase-B inhibitors

[Next question](#)

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline

- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

#### Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

#### COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

#### Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benztropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Which one of the following medications is most useful for helping to prevent attacks of Meniere's disease?

<input type="radio"/>	A. Promethazine
<input type="radio"/>	B. Prochlorperazine
<input type="radio"/>	C. Betahistine
<input type="radio"/>	D. Chlorphenamine
<input type="radio"/>	E. Cinnarizine

Next question

### Meniere's disease

Meniere's disease is a disorder of the inner ear of unknown cause. It is characterised by excessive pressure and progressive dilation of the endolymphatic system. It is more common in middle-aged adults but may be seen at any age. Meniere's disease has a similar prevalence in both men and women.

#### Features

- recurrent episodes of vertigo, tinnitus and hearing loss (sensorineural). Vertigo is usually the prominent symptom
- a sensation of aural fullness or pressure is now recognised as being common
- other features include nystagmus and a positive Romberg test
- episodes last minutes to hours
- typically symptoms are unilateral but bilateral symptoms may develop after a number of years

#### Natural history

- symptoms resolve in the majority of patients after 5-10 years
- some patients may be left with hearing loss
- psychological distress is common

#### Management

- ENT assessment is required to confirm the diagnosis
- patients should inform the DVLA. The current advice is to cease driving until satisfactory control of symptoms is achieved
- acute attacks: buccal or intramuscular prochlorperazine. Admission is sometimes required
- prevention: betahistine may be of benefit

A 23-year-old man with a history of migraine presents for review. His headaches are now occurring about once a week. He describes unilateral, throbbing headaches that may last over 24 hours. Neurological examination is unremarkable. Other than a history of asthma he is fit and well. What is the most suitable therapy to reduce the frequency of migraine attacks?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Propranolol   |
| <input type="radio"/> | B. Zolmitriptan  |
| <input type="radio"/> | C. Topiramate    |
| <input type="radio"/> | D. Amitriptyline |
| <input type="radio"/> | E. Pizotifen     |

[Next question](#)

#### Migraine

- acute: triptan + NSAID or triptan + paracetamol
- prophylaxis: topiramate or propranolol

Pizotifen is used less commonly nowadays due to side-effects such as weight gain. Propranolol should be avoided in asthmatics.

#### Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. NICE produced guidelines in 2012 on the management of headache, including migraines.

##### Acute treatment

- first-line: offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol
- for young people aged 12-17 years consider a nasal triptan in preference to an oral triptan
- if the above measures are not effective or not tolerated offer a non-oral preparation of metoclopramide\* or prochlorperazine and consider adding a non-oral NSAID or triptan

##### Prophylaxis

- prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients.

- NICE advise either topiramate or propranolol 'according to the person's preference, comorbidities and risk of adverse events'. Propranolol should be used in preference to topiramate in women of child bearing age as it may be teratogenic and it can reduce the effectiveness of hormonal contraceptives
- if these measures fail NICE recommend 'a course of up to 10 sessions of acupuncture over 5-8 weeks' or gabapentin
- NICE recommend: 'Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people'
- for women with predictable menstrual migraine treatment NICE recommend either frovatriptan (2.5 mg twice a day) or zolmitriptan (2.5 mg twice or three times a day) as a type of 'mini-prophylaxis'
- pizotifen is no longer recommend. Adverse effects such as weight gain & drowsiness are common

\*caution should be exercised with young patients as acute dystonic reactions may develop



Which one of the following statements regarding the stopping of anti-epileptic drugs (AED) is most correct?

<input type="radio"/>	A. Can be considered if seizure free for > 5 years, with AEDs being stopped over 2-3 months
<input type="radio"/>	B. Can be considered if seizure free for > 2 years, with AEDs being stopped over 2-3 months
<input type="radio"/>	C. Can be considered if seizure free for > 1 year, with AEDs being stopped over 2-3 months
<input type="radio"/>	D. Can be considered if seizure free for > 5 years, with AEDs being stopped over 8-12 months
<input type="radio"/>	E. Can be considered if seizure free for > 1 year, with AEDs being stopped over 8-12 months

Next question

The above reflects 2004 NICE guidelines and should be done under the guidance of a specialist. Benzodiazepines should be withdrawn over a longer period.

### Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Generalised tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures\* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

#### Partial seizures

- carbamazepine
- second line: lamotrigine\*\*, sodium valproate

\*carbamazepine may actually exacerbate absence seizure

\*\*the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

A 24-year-old female presents to her GP due to increased frequency of migraine attacks. She is now having around four migraines per month. Which type of medication would it be most appropriate to prescribe to reduce the frequency of migraine attacks?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. Specific 5-HT <sub>2</sub> agonist |
| <input type="radio"/> | B. 5-HT <sub>1</sub> antagonist       |
| <input type="radio"/> | C. Tricyclic antidepressant           |
| <input type="radio"/> | D. Beta-blocker                       |
| <input type="radio"/> | E. Specific 5-HT <sub>1</sub> agonist |

[Next question](#)

#### Migraine

- acute: triptan + NSAID or triptan + paracetamol
- prophylaxis: topiramate or propranolol

Topiramate is also recommended by NICE as first-line prophylaxis against migraine. However, given that she is female and of child-bearing age a beta-blocker (such as propranolol) is a better choice.

#### Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. NICE produced guidelines in 2012 on the management of headache, including migraines.

##### Acute treatment

- first-line: offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol
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- if these measures fail NICE recommend 'a course of up to 10 sessions of acupuncture over 5-8 weeks' or gabapentin
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- pizotifen is no longer recommend. Adverse effects such as weight gain & drowsiness are common

\*caution should be exercised with young patients as acute dystonic reactions may develop

A 42-year-old woman with a history of myasthenia gravis is admitted to the Emergency Department. She is currently taking pyridostigmine but there has been a significant worsening of her symptoms following antibiotic treatment for a chest infection. On examination she is dyspnoeic and cyanotic with quiet breath sounds in both lungs. Other than respiratory support, what are the two treatments of choice?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. IV methylprednisolone or plasmapheresis              |
| <input type="radio"/> | B. IV methylprednisolone or intravenous immunoglobulins |
| <input type="radio"/> | C. Plasmapheresis or atropine                           |
| <input type="radio"/> | D. IV methylprednisolone or atropine                    |
| <input type="radio"/> | E. Plasmapheresis or intravenous immunoglobulins        |

[Next question](#)

This patient is having a myasthenic crisis. Opinions vary as to whether plasmapheresis or intravenous immunoglobulins should be given first-line. Plasmapheresis usually works quicker but involves more expensive equipment

### Myasthenia gravis

Myasthenia gravis is an autoimmune disorder resulting in insufficient functioning acetylcholine receptors. Antibodies to acetylcholine receptors are seen in 90% of cases\*. Myasthenia is more common in women (2:1)

The key feature is muscle fatigability - muscles become progressively weaker during periods of activity and slowly improve after periods of rest:

- extraocular muscle weakness: diplopia
- proximal muscle weakness: face, neck, limb girdle
- ptosis
- dysphagia

### Associations

- thymomas in 15%
- autoimmune disorders: pernicious anaemia, autoimmune thyroid disorders, rheumatoid, SLE
- thymic hyperplasia in 50-70%

### Investigations

- Tensilon test: IV edrophonium reduces muscle weakness temporarily
- CT thorax to exclude thymoma
- CK normal

## Management

- long-acting anticholinesterase e.g. Pyridostigmine
- immunosuppression: prednisolone initially
- thymectomy

## Management of myasthenic crisis

- plasmapheresis
- intravenous immunoglobulins

\*antibodies are less commonly seen in disease limited to the ocular muscles

Which one of the following anti-epileptic drugs is most likely to cause visual field defects?

<input type="radio"/>	A. Lamotrigine
<input type="radio"/>	B. Phenytoin
<input type="radio"/>	C. Ethosuximide
<input type="radio"/>	D. Vigabatrin
<input type="radio"/>	E. Pregabalin

Next question

V for Vigabatrin - V for Visual field defects

### Vigabatrin

#### Key points

- 40% of patients develop visual field defects, which may be irreversible
- visual fields should be checked every 6 months

A 55-year-old man presents complaining of visual disturbance. Examination reveals a right congruous homonymous hemianopia with macula sparing. Where is the lesion most likely to be?

<input type="radio"/>	A. Right optic nerve
<input type="radio"/>	B. Left optic radiation
<input type="radio"/>	C. Left optic tract
<input type="radio"/>	D. Left occipital cortex
<input type="radio"/>	E. Optic chiasm

Next question

Visual field defects:

- left homonymous hemianopia means visual field defect to the left, i.e. lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

### Visual field defects

The main points for the exam are:

- left homonymous hemianopia means visual field defect to the left, i.e. Lesion of right optic tract
- homonymous quadrantanopias: PITS (Parietal-Inferior, Temporal-Superior)
- incongruous defects = optic tract lesion; congruous defects = optic radiation lesion or occipital cortex

A congruous defect simply means complete or symmetrical visual field loss and conversely an incongruous defect is incomplete or asymmetric. Please see the link for an excellent diagram.

Homonymous hemianopia

- incongruous defects: lesion of optic tract
- congruous defects: lesion of optic radiation or occipital cortex
- macula sparing: lesion of occipital cortex

Homonymous quadrantanopias\*

- superior: lesion of temporal lobe
- inferior: lesion of parietal lobe



- mnemonic = PITS (Parietal-Inferior, Temporal-Superior)

#### Bitemporal hemianopia

- lesion of optic chiasm
- upper quadrant defect > lower quadrant defect = inferior chiasmal compression, commonly a pituitary tumour
- lower quadrant defect > upper quadrant defect = superior chiasmal compression, commonly a craniopharyngioma

\*this is very much the 'exam answer'. Actual studies suggest that the majority of quadrantanopias are caused by occipital lobe lesions. Please see the following link for more details:

<http://www.ncbi.nlm.nih.gov/pubmed/9109741>

A 65-year-old female is admitted with a right hemiparesis. Examination reveals she is in atrial fibrillation. CT confirms an ischaemic stroke and aspirin 300mg is commenced. If the patient is well and develops no new problems at what point should warfarin be started?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. After 14 days   |
| <input type="radio"/> | B. Immediately   |
| <input type="radio"/> | C. After 7 days  |
| <input type="radio"/> | D. Following a repeat CT at 28 days to exclude secondary haemorrhage |
| <input type="radio"/> | E. Following a repeat CT at 14 days to exclude secondary haemorrhage |

[Next question](#)

The 2004 RCP guidelines recommend that anticoagulation should be commenced 14 days after an ischaemic stroke. Earlier anticoagulation may exacerbate any secondary haemorrhage

### Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued stroke guidelines in 2008, although they modified their guidance with respect to antiplatelet therapy in 2010.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy\*
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commenced on a statin. Many physicians will delay treatment until after at least 48 hours due to the risk of haemorrhagic transformation

### Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 hours\*\* of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

## Secondary prevention

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- clopidogrel is now recommended by NICE ahead of combination use of aspirin plus modified release (MR) dipyridamole in people who have had an ischaemic stroke
- aspirin plus MR dipyridamole is now recommended after an ischaemic stroke only if clopidogrel is contraindicated or not tolerated, but treatment is no longer limited to 2 years' duration
- MR dipyridamole alone is recommended after an ischaemic stroke only if aspirin or clopidogrel are contraindicated or not tolerated, again with no limit on duration of treatment

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST\*\*\* criteria or > 50% according to NASCET\*\*\*\* criteria

\*the 2009 Controlling hypertension and hypotension immediately post-stroke (CHHIPS) trial may change thinking on this but guidelines have yet to change to reflect this

\*\*SIGN recommend a window of 4.5 hours

\*\*\*European Carotid Surgery Trialists' Collaborative Group

\*\*\*\*North American Symptomatic Carotid Endarterectomy Trial

Which one of the following statements regarding restless legs syndrome is incorrect?

<input type="radio"/>	A. Movements may be seen during sleep
<input type="radio"/>	B. May be secondary to uraemia
<input type="radio"/>	C. Affects approximately 5% of the general population
<input type="radio"/>	D. Family history is found in up to 50% of patients
<input type="radio"/>	E. It is three times as common in females

Next question

Males and females are thought to be equally affected, with only one study showing a slightly increased incidence in females

### Restless legs syndrome

Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. It is extremely common, affecting between 2-10% of the general population. Males and females are equally affected and a family history may be present

#### Clinical features

- uncontrollable urge to move legs (akathisia). Symptoms initially occur at night but as condition progresses may occur during the day. Symptoms are worse at rest
- paraesthesias e.g. 'crawling' or 'throbbing' sensations
- movements during sleep may be noted by the partner - periodic limb movements of sleep (PLMS)

#### Causes and associations

- there is a positive family history in 50% of patients with idiopathic RLS
- iron deficiency anaemia
- uraemia
- diabetes mellitus
- pregnancy

The diagnosis is clinical although bloods to exclude iron deficiency anaemia may be appropriate

#### Management

- simple measures: walking, stretching, massaging affected limbs
- treat any iron deficiency
- dopamine agonists are first-line treatment (e.g. Pramipexole, ropinirole)
- benzodiazepines
- gabapentin

Which one of the following conditions is least recognised as a cause of a seventh nerve palsy?

<input type="radio"/>	A. Acoustic neuroma
<input type="radio"/>	B. Herpes zoster
<input type="radio"/>	C. HIV
<input type="radio"/>	D. Systemic lupus erythematosus
<input type="radio"/>	E. Diabetes mellitus

Next question

## Facial nerve

Supply - 'face, ear, taste, tear'

- face: muscles of facial expression
- ear: nerve to stapedius
- taste: supplies anterior two-thirds of tongue
- tear: parasympathetic fibres to lacrimal glands, also salivary glands

Causes of bilateral facial nerve palsy

- sarcoidosis
- Guillain-Barre syndrome
- polio, Lyme disease

Causes of unilateral facial nerve palsy - as above plus

Lower motor neuron	Upper motor neuron
<ul style="list-style-type: none"> <li>• Bell's palsy</li> <li>• Ramsay-Hunt syndrome (due to herpes zoster)</li> <li>• acoustic neuroma</li> <li>• parotid tumours</li> <li>• HIV</li> <li>• multiple sclerosis*</li> <li>• diabetes mellitus</li> </ul>	<ul style="list-style-type: none"> <li>• stroke</li> </ul>

LMN vs. UMN

- upper motor neuron lesion 'spares' upper face i.e. forehead
- lower motor neuron lesion affects all facial muscles

\*may also cause an UMN palsy

A 45-year-old female is diagnosed with a glioma in the parietal lobe after being investigated for new onset seizures. Which one of the following features is she most likely to develop?

<input type="radio"/>	A. Visual agnosia
<input type="radio"/>	B. Auditory agnosia
<input type="radio"/>	C. Acalculia
<input type="radio"/>	D. Inability to generate a list
<input type="radio"/>	E. Expressive (Broca's) aphasia

[Next question](#)

## Brain lesions

The following neurological disorders/features may allow localisation of a brain lesion:

### Gross anatomy

#### Parietal lobe lesions

- sensory inattention
- apraxias
- astereognosis (tactile agnosia)
- inferior homonymous quadrantanopia
- Gerstmann's syndrome (lesion of dominant parietal): alexia, acalculia, finger agnosia and right-left disorientation

#### Occipital lobe lesions

- homonymous hemianopia (with macula sparing)
- cortical blindness
- visual agnosia

#### Temporal lobe lesion

- Wernicke's aphasia
- superior homonymous quadrantanopia
- auditory agnosia
- prosopagnosia (difficulty recognising faces)

## Frontal lobes lesions

- expressive (Broca's) aphasia: located on the posterior aspect of the frontal lobe, in the inferior frontal gyrus
- disinhibition
- perseveration
- anosmia
- inability to generate a list

## Cerebellum lesions

- midline lesions: gait and truncal ataxia
- hemisphere lesions: intention tremor, past pointing, dysdiadokinesis, nystagmus

## More specific areas

Medial thalamus and mammillary bodies of the hypothalamus	Wernicke and Korsakoff syndrome
Subthalamic nucleus of the basal ganglia	Hemiballism
Striatum (caudate nucleus) of the basal ganglia	Huntington chorea
Substantia nigra of the basal ganglia	Parkinson's disease
Amygdala	KluverBucy syndrome (hypersexuality, hyperorality, hyperphagia, visual agnosia)

A 71-year-old man is admitted to the Emergency Department. His family report that since yesterday he has been very 'clumsy' and unsteady on his feet. This morning he started to complain of numbness down his left side. On examination you notice that he has a right-sided Horner's syndrome and horizontal nystagmus. Examination of the peripheral nervous system confirms the sensory loss on the left side. Where is the lesion most likely to be?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Lateral sinus thrombosis             |
| <input type="radio"/> | B. Posterior cerebral artery            |
| <input type="radio"/> | C. Posterior inferior cerebellar artery |
| <input type="radio"/> | D. Middle cerebral artery               |
| <input type="radio"/> | E. Anterior inferior cerebellar artery  |

[Next question](#)

### Lateral medullary syndrome

Lateral medullary syndrome, also known as Wallenberg's syndrome, occurs following occlusion of the posterior inferior cerebellar artery

#### Cerebellar features

- ataxia
- nystagmus

#### Brainstem features

- ipsilateral: dysphagia, facial numbness, cranial nerve palsy e.g. Horner's
- contralateral: limb sensory loss



A 76-year-old man is admitted with a right hemiparesis. On examination his blood pressure is 120/78 mmHg, pulse 84 bpm and oxygen saturations 96% on room air. A CT scan excludes intracerebral haemorrhage and he is given aspirin 300mg. What is the most appropriate management with regards to oxygen therapy in the first 12 hours following admission?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. 35% via Venturi mask               |
| <input type="radio"/> | B. 24% via Venturi mask               |
| <input type="radio"/> | C. No oxygen therapy                  |
| <input type="radio"/> | D. 28% via Venturi mask               |
| <input type="radio"/> | E. 2 litres/minute via nasal cannulae |

[Next question](#)

Both the NICE stroke guidelines and British Thoracic Society oxygen guidelines do not support giving oxygen in this scenario.

### Oxygen therapy

The British Thoracic Society published guidelines on emergency oxygen therapy in 2008. The following selected points are taken from the guidelines. Please see the link provided for the full guideline.

**In patients who are critically ill (anaphylaxis, shock etc) oxygen should initially be given via a reservoir mask at 15 l/min. Hypoxia kills.** The BTS guidelines specifically exclude certain conditions where the patient is acutely unwell (e.g. myocardial infarction) but stable.

#### Oxygen saturation targets

- acutely ill patients: 94-98%
- patients at risk of hypercapnia (e.g. COPD patients): 88-92% (see below)
- oxygen should be reduced in stable patients with satisfactory oxygen saturation

#### Management of COPD patients

- prior to availability of blood gases, use a 28% Venturi mask at 4 l/min and aim for an oxygen saturation of 88-92% for patients with risk factors for hypercapnia but no prior history of respiratory acidosis
- adjust target range to 94-98% if the pCO<sub>2</sub> is normal

Situations where oxygen therapy should not be used routinely if there is no evidence of hypoxia:

- myocardial infarction and acute coronary syndromes
- stroke
- obstetric emergencies
- anxiety-related hyperventilation

A 23-year-old female has a lumbar puncture to exclude a subarachnoid haemorrhage following a negative CT scan. Which one of the following factors would be most likely to influence the incidence of post-lumbar puncture headache?

<input type="radio"/>	A. Position of the patient
<input type="radio"/>	B. Increased fluid intake post procedure
<input type="radio"/>	C. Opening pressure of CSF
<input type="radio"/>	D. Bed rest following the procedure
<input type="radio"/>	E. Replacing the stylet

Next question

### Post-lumbar puncture headache

Headache following lumbar puncture (LP) occurs in approximately one-third of patients. The pathophysiology of is unclear but may relate to a 'leak' of CSF following dural puncture. Post-LP headaches are more common in young females with a low body mass index

#### Typical features

- usually develops within 24-48 hours following LP but may occur up to one week later
- may last several days
- worsens with upright position
- improves with recumbent position

Factors which may contribute to headache	Factors which do not contribute to headache
Increased needle size Direction of bevel Not replacing the stylet Increased number of LP attempts	Increased volume of CSF removed Bed rest following procedure Increased fluid intake post procedure Opening pressure of CSF Position of patient

#### Management

- supportive initially (analgesia, rest)
- if pain continues for more than 72 hours then specific treatment is indicated, to prevent subdural haematoma
- treatment options include: blood patch, epidural saline and intravenous caffeine

A 64-year-old man who is under investigation for parkinsonian symptoms is brought to the GP by his wife. She is concerned her husband is becoming increasingly agitated. The GP prescribes haloperidol. One week later the GP is called out to see the patient as his parkinsonian symptoms have deteriorated markedly. What is the most likely underlying diagnosis?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Lewy body dementia             |
| <input type="radio"/> | B. Normal pressure hydrocephalus  |
| <input type="radio"/> | C. Progressive supranuclear palsy |
| <input type="radio"/> | D. Multiple system atrophy        |
| <input type="radio"/> | E. Dementia pugilistica           |

[Next question](#)

Patients with Lewy body dementia are extremely sensitive to neuroleptic agents

### Lewy body dementia

Lewy body dementia is an increasingly recognised cause of dementia, accounting for up to 20% of cases. The characteristic pathological feature is alpha-synuclein cytoplasmic inclusions (Lewy bodies) in the substantia nigra, paralimbic and neocortical areas

The relationship between Parkinson's disease and Lewy body dementia is complicated, particularly as dementia is often seen in Parkinson's disease. Also, up to 40% of patients with Alzheimer's have Lewy bodies

Neuroleptics should be avoided in Lewy body dementia as patients are extremely sensitive and may develop irreversible parkinsonism. Questions may give a history of a patient who has deteriorated following the introduction of an antipsychotic agent

#### Features

- progressive cognitive impairment
- parkinsonism
- visual hallucinations (other features such as delusions and non-visual hallucinations may also be seen)

A 62-year-old man is seen in the rapid access transient ischaemic attack clinic following three episodes over the past two weeks of transient left sided weakness. What is the most appropriate advice to give with regards to driving?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Cannot drive for 12 months                 |
| <input type="radio"/> | B. Cannot drive until investigations complete |
| <input type="radio"/> | C. Inform DVLA but can continue driving       |
| <input type="radio"/> | D. Cannot drive for 3 months                  |
| <input type="radio"/> | E. Cannot drive for 1 month                   |

[Next question](#)

DVLA advice post multiplier TIAs: cannot drive for 3 months

### DVLA: neurological disorders

The guidelines below relate to car/motorcycle use unless specifically stated. For obvious reasons, the rules relating to drivers of heavy goods vehicles tend to be much stricter

#### Specific rules

- first seizure: 6 months off driving\*. For patients with established epilepsy they must be fit free for 12 months before being able to drive
- stroke or TIA: 1 month off driving
- multiple TIAs over short period of times: 3 months off driving
- craniotomy e.g. For meningioma: 1 year off driving\*\*
- pituitary tumour: craniotomy: 6 months; trans-sphenoidal surgery 'can drive when there is no debarring residual impairment likely to affect safe driving'
- narcolepsy/cataplexy: cease driving on diagnosis, can restart once 'satisfactory control of symptoms'

#### Syncope

- simple faint: no restriction
- unexplained, low risk of recurrence: 4 weeks off
- explained and treated: 4 weeks off
- unexplained: 6 months off

\*previously rule was 12 months. It is now 6 months off driving if the licence holder has undergone assessment by

an appropriate specialist and no relevant abnormality has been identified on investigation, for example EEG and brain scan where indicated

\*\*if the tumour is a benign meningioma and there is no seizure history, licence can be reconsidered 6 months after surgery if remains seizure free

A 73-year-old woman presents with episodic confusion and headaches for the past week. She has a history of alcohol excess and a background of atrial fibrillation and type 2 diabetes mellitus. Her daughter reports that she has been having frequent spells of confusion over the past few days. Last year she was assessed for frequent falls. Her current medications include bisoprolol, metformin and warfarin. Neurological examination is unremarkable and her blood sugar is 6.7 mmol/l. What is the most likely diagnosis?

- ☐ A. Korsakoff's syndrome
- ☐ B. Wernicke's encephalopathy
- ☐ C. Extradural haematoma
- ☐ D. Subarachnoid haemorrhage
- ☐ E. Subdural haematoma

[Next question](#)

Fluctuating confusion/consciousness? - subdural haematoma

This patient has a number of risk factors for a subdural haematoma including old age, alcoholism and anticoagulation. Korsakoff's syndrome and Wernicke's encephalopathy do not usually cause headaches.

## Head injury

Types of traumatic brain injury:

<b>Extradural (epidural) haematoma</b>	<p>Bleeding into the space between the dura mater and the skull. Often results from acceleration-deceleration trauma or a blow to the side of the head. The majority of epidural haematomas occur in the temporal region where skull fractures cause a rupture of the middle meningeal artery.</p> <p>Features</p> <ul style="list-style-type: none"> <li>• features of raised intracranial pressure</li> <li>• some patients may exhibit a lucid interval</li> </ul>
<b>Subdural haematoma</b>	<p>Bleeding into the outermost meningeal layer. Most commonly occur around the frontal and parietal lobes.</p> <p>Risk factors include old age, alcoholism and anticoagulation.</p> <p>Slower onset of symptoms than a epidural haematoma.</p>
<b>Subarachnoid haemorrhage</b>	<p>Usually occurs spontaneously in the context of a ruptured cerebral aneurysm but may be seen in association with other injuries when a patient has sustained a traumatic brain injury</p>

A 34-year-old man who is known to suffer from complex partial seizures is reviewed in the neurology clinic. He has not been able to tolerate either carbamazepine or sodium valproate. What is the most appropriate next line drug?

<input type="radio"/>	A. Phenytoin
<input type="radio"/>	B. Lamotrigine
<input type="radio"/>	C. Ethosuximide
<input type="radio"/>	D. Topiramate
<input type="radio"/>	E. Clonazepam

[Next question](#)

### Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

Generalised tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

Absence seizures\* (Petit mal)

- sodium valproate or ethosuximide
- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

## Partial seizures

- carbamazepine
- second line: lamotrigine\*\*, sodium valproate

\*carbamazepine may actually exacerbate absence seizure

\*\*the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines



### Question 165 of 204

Next

A 31-year-old woman presents with a 4 month history of headache. She has brought a headache diary which demonstrates that her symptoms are present on around 20-25 days of each month. The headache is typically unilateral and she is currently taking paracetamol 1g qds and ibuprofen 400mg tds everyday to try and relieve her symptoms. A diagnosis of medication overuse headache is suspected. What is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Add metoclopramide + start propranolol            |
| <input type="radio"/> | B. Gradually withdraw analgesics + start propranolol |
| <input type="radio"/> | C. Abruptly stop analgesics                          |
| <input type="radio"/> | D. Gradually withdraw analgesics                     |
| <input type="radio"/> | E. Continue analgesics + start propranolol           |

Next question

#### Medication overuse headache

- simple analgesia + triptans: stop abruptly
- opioid analgesia: withdraw gradually

This answer may seem counterintuitive but it is line with recent guidelines from SIGN, please see the link provided.

#### Medication overuse headache

Medication overuse headache is one of the most common causes of chronic daily headache. It may affect up to 1 in 50 people

#### Features

- present for 15 days or more per month
- developed or worsened whilst taking regular symptomatic medication
- patients using opioids and triptans are at most risk
- may be psychiatric co-morbidity

#### Management (from 2008 SIGN guidelines)

- simple analgesics and triptans should be withdrawn abruptly (may initially worsen headaches)
- opioid analgesics should be gradually withdrawn

Which one of the following is least likely to produce a lymphocytosis in the cerebrospinal fluid?

<input type="radio"/>	A. Systemic lupus erythematosus
<input type="radio"/>	B. Guillain-Barre syndrome
<input type="radio"/>	C. Viral encephalitis
<input type="radio"/>	D. Partially treated bacterial meningitis
<input type="radio"/>	E. Behcet's syndrome

Next question

### Cerebrospinal fluid: raised lymphocytes

Normal values of cerebrospinal fluid (CSF) are as follows:

- pressure = 60-150 mm (patient recumbent)
- protein = 0.2-0.4 g/l
- glucose =  $> 2/3$  blood glucose
- cells: red cells = 0, white cells  $< 5/\text{mm}^3$

The following conditions are associated with raised lymphocytes

- viral meningitis/encephalitis
- TB meningitis
- partially treated bacterial meningitis
- Lyme disease
- Behcet's, SLE
- lymphoma, leukaemia

Which of the following features is least likely to be found in a patient with tuberous sclerosis?

<input type="radio"/>	A. Shagreen patches
<input type="radio"/>	B. Café-au-lait spots
<input type="radio"/>	C. Retinal hamartomas
<input type="radio"/>	D. Axillary freckling
<input type="radio"/>	E. Renal angiomyolipomata

Next question

Axillary freckling is seen in neurofibromatosis

### Tuberous sclerosis

Tuberous sclerosis (TS) is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in TS are neuro-cutaneous

#### Cutaneous features

- depigmented 'ash-leaf' spots which fluoresce under UV light
- roughened patches of skin over lumbar spine (Shagreen patches)
- adenoma sebaceum: butterfly distribution over nose
- fibromata beneath nails (subungual fibromata)
- café-au-lait spots\* may be seen

#### Neurological features

- developmental delay
- epilepsy (infantile spasms or partial)
- intellectual impairment

#### Also

- retinal hamartomas: dense white areas on retina (phakomata)
- rhabdomyomas of the heart
- gliomatous changes can occur in the brain lesions
- polycystic kidneys, renal angiomyolipomata

\*these of course are more commonly associated with neurofibromatosis. However a 1998 study of 106 children with TS found café-au-lait spots in 28% of patients

### Question 168 of 204

Neuropathic pain characteristically responds poorly to opioids. However, if standard treatment options have failed which opioid is it most appropriate to consider starting?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Tramadol      |
| <input type="radio"/> | B. Morphine      |
| <input type="radio"/> | C. Codeine       |
| <input type="radio"/> | D. Oxycodone     |
| <input type="radio"/> | E. Buprenorphine |

[Next question](#)

### Neuropathic pain

Neuropathic pain may be defined as pain which arises following damage or disruption of the nervous system. It is often difficult to treat and responds poorly to standard analgesia.

Examples include:

- diabetic neuropathy
- post-herpetic neuralgia
- trigeminal neuralgia
- prolapsed intervertebral disc

NICE issued guidance in 2010 on the management of neuropathic pain:

- first-line treatment\*: oral amitriptyline or pregabalin
- if satisfactory pain reduction is obtained with amitriptyline but the person cannot tolerate the adverse effects, consider oral imipramine or nortriptyline as an alternative
- second-line treatment: if first-line treatment was with amitriptyline, switch to or combine with pregabalin. If first-line treatment was with pregabalin, switch to or

combine with amitriptyline

- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

\*please note that for some specific conditions the guidance may vary. For example carbamazepine is used first-line for trigeminal neuralgia, duloxetine for diabetic neuropathy

A 65-year-old man who is known to have metastatic colorectal cancer presents for review. Since last been seen he reports being generally stiff and on examination is noted to have diffuse hypertonia. Which antibodies are most likely to be responsible for this presentation?

<input type="radio"/>	A. Anti-GAD
<input type="radio"/>	B. Anti-Ri
<input type="radio"/>	C. Anti-Hu
<input type="radio"/>	D. Anti-La
<input type="radio"/>	E. Anti-Yo

[Next question](#)

This patient has developed stiff person's syndrome.

### Paraneoplastic syndromes affecting nervous system

#### Lambert-Eaton myasthenic syndrome

- associated with small cell lung cancer (also breast and ovarian)
- antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system
- can also occur independently as autoimmune disorder

#### Anti-Hu

- associated with small cell lung carcinoma and neuroblastomas
- sensory neuropathy - may be painful
- cerebellar syndrome
- encephalomyelitis

#### Anti-Yo

- associated with ovarian and breast cancer
- cerebellar syndrome

#### Anti-GAD antibody

- associated with breast, colorectal and small cell lung carcinoma
- stiff person's syndrome or diffuse hypertonia

#### Anti-Ri

- associated with breast and small cell lung carcinoma
- ocular opsoclonus-myoclonus

Which one of the following factors indicates a poor prognosis in patients with multiple sclerosis?

<input type="radio"/>	A. Relapsing-remitting disease
<input type="radio"/>	B. Presence of sensory symptoms
<input type="radio"/>	C. Young age of onset
<input type="radio"/>	D. Male sex
<input type="radio"/>	E. Long interval between first two relapses

Next question

### Multiple sclerosis: prognostic features

Good prognosis features

- female sex
- young age of onset
- relapsing-remitting disease
- sensory symptoms
- long interval between first two relapses

Ways of remembering prognostic features

- the typical patient carries a better prognosis than an atypical presentation

A 24-year-old woman with Charcot-Marie-Tooth disease (type 1) asks how likely it is that any future children will have the disease. What is the most accurate answer?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Three times as likely as background population |
| <input type="radio"/> | B. 25%  |
| <input type="radio"/> | C. Between 5 - 10%                                |
| <input type="radio"/> | D. Same as background population                  |
| <input type="radio"/> | E. 50%  |

[Next question](#)

Charcot-Marie-Tooth disease (hereditary sensorimotor neuropathy type I) is an autosomal dominant condition and therefore 50% of children will be affected

### HSMN

Hereditary sensorimotor neuropathy (HSMN) is a relatively new term which encompasses Charcot-Marie-Tooth disease (also known as peroneal muscular atrophy). Over 7 types have been characterised - however only 2 are common to clinical practice

- HSMN type I: primarily due to demyelinating pathology
- HSMN type II: primarily due to axonal pathology

#### HSMN type I

- autosomal dominant
- due to defect in PMP-22 gene (which codes for myelin)
- features often start at puberty
- motor symptoms predominate
- distal muscle wasting, pes cavus, clawed toes
- foot drop, leg weakness often first features

A 44-year-old woman presents with a three month history of worsening involuntary movements of the head. These are worse when she is stressed and improved by alcohol. They are not present when she is sleep. There are no other neurological symptoms of note and neurological examination is unremarkable other than spontaneous movements of the head which are worse when she looks to either side. Her father had a similar complaint but never sought medical attention. What is the most likely diagnosis?

<input type="radio"/>	A. Parkinson's disease
<input type="radio"/>	B. Cerebellar tremor
<input type="radio"/>	C. Huntington's disease
<input type="radio"/>	D. Multiple sclerosis
<input type="radio"/>	E. Essential tremor

[Next question](#)

Essential tremor is the most common cause of titubation (head tremor). Whilst the majority of patients will complain of hand tremor titubation may occur in isolation. The tremor is characteristic as it is worse on movement and during stress and relieved by alcohol and sleep. The family history is also a pointer.

### Essential tremor

Essential tremor (previously called benign essential tremor) is an autosomal dominant condition which usually affects both upper limbs

#### Features

- postural tremor: worse if arms outstretched
- improved by alcohol and rest
- most common cause of titubation (head tremor)

#### Management

- propranolol is first-line
- primidone is sometimes used



A 40-year-old woman who is known to be HIV positive is admitted to the Emergency Department following a seizure. Her partner reports that she has been having headaches, night sweats and a poor appetite for the past four weeks. Blood tests and a CT head are arranged:

CD4	89 u/l
CT head	Single ring-enhancing lesion in the right parietal lobe

What is the most likely diagnosis?

<input type="radio"/>	A. Primary CNS lymphoma
<input type="radio"/>	B. Tuberculosis
<input type="radio"/>	C. Progressive multifocal leukoencephalopathy
<input type="radio"/>	D. <i>Cryptococcus</i>
<input type="radio"/>	E. Toxoplasmosis

Next question

This is a difficult question. Toxoplasmosis is the most common cause of brain lesions in HIV patients. However, around 80% of toxoplasmosis cases involve multiple lesions and the history is suggestive of lymphoma. Cerebral tuberculosis is much less common than lymphoma in HIV.

### HIV: neurocomplications

#### Generalised neurological disease

##### Encephalitis

- may be due to CMV or HIV itself
- HSV encephalitis but is relatively rare in the context of HIV
- CT: oedematous brain

##### *Cryptococcus*

- most common fungal infection of CNS
- headache, fever, malaise, nausea/vomiting, seizures, focal neurological deficit
- CSF: high opening pressure, India ink test positive
- CT: meningeal enhancement, cerebral oedema
- meningitis is typical presentation but may occasionally cause a space occupying lesion

##### Progressive multifocal leukoencephalopathy (PML)

- widespread demyelination

- due to infection of oligodendrocytes by human papovirus (JC virus)
- symptoms, subacute onset : behavioural changes, speech, motor, visual impairment
- CT: single or multiple lesions, no mass effect, don't usually enhance. MRI is better - high-signal demyelinating white matter lesions are seen

#### AIDS dementia complex

- caused by HIV virus itself
- symptoms: behavioural changes, motor impairment
- CT: cortical and subcortical atrophy

### Focal neurological lesions

#### Toxoplasmosis

- accounts for around 50% of cerebral lesions in patients with HIV
- constitutional symptoms, headache, confusion, drowsiness
- CT: usually single or multiple ring enhancing lesions, mass effect may be seen
- management: sulfadiazine and pyrimethamine

#### Primary CNS lymphoma

- accounts for around 30% of cerebral lesions
- associated with the Epstein-Barr virus
- CT: single or multiple ring enhancing lesions

Differentiating between toxoplasmosis and lymphoma is a common clinical scenario in HIV patients. It is clearly important given the vastly different treatment strategies. The table below gives some general differences. Please see the Radiopaedia link for more details.

Toxoplasmosis	Lymphoma
Multiple lesions	Single lesion
Rng or nodular enhancement	Solid enhancement
Thallium SPECT negative	Thallium SPECT positive

#### Tuberculosis

- much less common than toxoplasmosis or primary CNS lymphoma
- CT: single enhancing lesion

Which one of the following statements regarding the use of 5-HT<sub>1</sub> agonists in the treatment of migraine is incorrect?

<input type="radio"/>	A. May be given subcutaneously
<input type="radio"/>	B. Are second line therapy in the management of acute migraine
<input type="radio"/>	C. Should be taken as soon as possible after the onset of an aura
<input type="radio"/>	D. Should be avoided in patients with ischaemic heart disease
<input type="radio"/>	E. Adverse effects include tingling and chest tightness

Next question

Triptans should be taken when the headache starts, rather than the aura

### Triptans

Triptans are specific 5-HT<sub>1</sub> agonists used in the acute treatment of migraine. They are generally used second line when standard analgesics such as paracetamol and ibuprofen are ineffective.

Prescribing points

- should be taken as soon as possible after the onset of headache, rather than at onset of aura
- oral, orodispersible, nasal spray and subcutaneous injections are available

Adverse effects

- 'triptan sensations' - tingling, heat, tightness (e.g. throat and chest), heaviness, pressure

Contraindications

- patients with a history of, or significant risk factors for, ischaemic heart disease or cerebrovascular disease

Which one of the following statements regarding epilepsy in pregnant women is correct?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. All pregnant women on antiepileptic medication should take 400mcg a day of folic acid    |
| <input type="radio"/> | B. Antiepileptic drug levels should be monitored throughout pregnancy                       |
| <input type="radio"/> | C. The dose of lamotrigine usually needs to be decreased during pregnancy                   |
| <input type="radio"/> | D. Pregnant women taking phenytoin should be given vitamin K in the last month of pregnancy |
| <input type="radio"/> | E. Sodium valproate is most strongly associated with cleft palate                           |

Next question

### Epilepsy: pregnancy and breast feeding

The risks of uncontrolled epilepsy during pregnancy generally outweigh the risks of medication to the fetus. All women thinking about becoming pregnant should be advised to take folic acid 5mg per day well before pregnancy to minimise the risk of neural tube defects. Around 1-2% of newborns born to non-epileptic mothers have congenital defects. This rises to 3-4% if the mother takes antiepileptic medication.

Other points

- aim for monotherapy
- there is no indication to monitor antiepileptic drug levels
- sodium valproate: associated with neural tube defects
- carbamazepine: often considered the least teratogenic of the older antiepileptics
- phenytoin: associated with cleft palate
- lamotrigine: studies to date suggest the rate of congenital malformations may be low. The dose of lamotrigine may need to be increased in pregnancy

Breast feeding is generally considered safe for mothers taking antiepileptics with the possible exception of the barbiturates

It is advised that pregnant women taking phenytoin are given vitamin K in the last month of pregnancy to prevent clotting disorders in the newborn

A 37-year-old woman with a history of type 2 diabetes mellitus and obesity presents after a late period. The urinary hCG test is positive. Her current medication is as follows:

Orlistat 120mg tds  
Simvastatin 40mg on  
Aspirin 75mg od  
Metformin 1g bd  
Paracetamol 1g qds  
Aqueous cream prn

Which one of her medications must be stopped straight away?

- |                       |                |
|-----------------------|----------------|
| <input type="radio"/> | A. Paracetamol |
| <input type="radio"/> | B. Aspirin     |
| <input type="radio"/> | C. Simvastatin |
| <input type="radio"/> | D. Orlistat    |
| <input type="radio"/> | E. Metformin   |

Next question

Simvastatin is contraindicated in pregnancy and must be stopped immediately. Metformin is sometimes used in pregnancy although many diabetic women are converted to insulin for the duration of the pregnancy to try and maximise control and minimise complications.

Whilst orlistat is not a known teratogen it should be used with 'caution' in pregnancy according to the BNF and the benefits are very likely outweighed by risks.

### Prescribing in pregnant patients

Very few drugs are known to be completely safe in pregnancy. The list below largely comprises of those known to be harmful. Some countries have developed a grading system - see the link.

#### Antibiotics

- tetracyclines
- aminoglycosides
- sulphonamides and trimethoprim
- quinolones: the BNF advises to avoid due to arthropathy in some animal studies

#### Other drugs

- ACE inhibitors, angiotensin II receptor antagonists
- statins
- warfarin

- sulfonylureas
- retinoids (including topical)
- cytotoxic agents

The majority of antiepileptics including valproate, carbamazepine and phenytoin are known to be potentially harmful. The decision to stop such treatments however is difficult as uncontrolled epilepsy is also a risk

A 22-year-old female presents with a history of fits, describing focal seizures associated with impairment of consciousness. What is the most suitable first-line treatment?

<input type="radio"/>	A. Phenytoin
<input type="radio"/>	B. Sodium valproate
<input type="radio"/>	C. Gabapentin
<input type="radio"/>	D. Levetiracetam
<input type="radio"/>	E. Carbamazepine

[Next question](#)

#### Epilepsy medication: first-line

- generalised seizure: sodium valproate
- partial seizure: carbamazepine

The 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines

#### Epilepsy: treatment

Most neurologists now start antiepileptics following a second epileptic seizure. NICE guidelines suggest starting antiepileptics after the first seizure if any of the following are present:

- the patient has a neurological deficit
- brain imaging shows a structural abnormality
- the EEG shows unequivocal epileptic activity
- the patient or their family or carers consider the risk of having a further seizure unacceptable

Sodium valproate is considered the first line treatment for patients with generalised seizures with carbamazepine used for partial seizures

#### Generalised tonic-clonic seizures

- sodium valproate
- second line: lamotrigine, carbamazepine

#### Absence seizures\* (Petit mal)

- sodium valproate or ethosuximide

- sodium valproate particularly effective if co-existent tonic-clonic seizures in primary generalised epilepsy

#### Myoclonic seizures

- sodium valproate
- second line: clonazepam, lamotrigine

#### Partial seizures

- carbamazepine
- second line: lamotrigine\*\*, sodium valproate

\*carbamazepine may actually exacerbate absence seizure

\*\*the 2007 SANAD study indicated that lamotrigine may be a more suitable first-line drug for partial seizures although this has yet to work its way through to guidelines



Which one of the following is least recognised as causing idiopathic intracranial hypertension?

<input type="radio"/>	A. Oral contraceptive pill
<input type="radio"/>	B. Tetracycline
<input type="radio"/>	C. Ciclosporin
<input type="radio"/>	D. Prednisolone
<input type="radio"/>	E. Vitamin A

Next question

### Idiopathic intracranial hypertension

Idiopathic intracranial hypertension (also known as pseudotumour cerebri and formerly benign intracranial hypertension) is a condition classically seen in young, overweight females.

#### Features

- headache
- blurred vision
- papilloedema (usually present)
- enlarged blind spot
- sixth nerve palsy may be present

#### Risk factors

- obesity
- female sex
- pregnancy
- drugs\*: oral contraceptive pill, steroids, tetracycline, vitamin A

#### Management

- weight loss
- diuretics e.g. acetazolamide
- repeated lumbar puncture
- surgery: optic nerve sheath decompression and fenestration may be needed to prevent damage to the optic nerve. A lumboperitoneal or ventriculoperitoneal shunt may also be performed to reduce intracranial pressure

\*if intracranial hypertension is thought to occur secondary to a known causes (e.g. Medication) then it is of course not idiopathic

### Question 179 of 204

A 19-year-old presents as she would like to start a combined oral contraceptive pill. During the history she states that in the past she has had migraine with aura. She asks why the combined oral contraceptive pill is contraindicated. What is the most appropriate response?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Theoretical risk of ischaemic stroke                              |
| <input type="radio"/> | B. Significantly increased risk of ischaemic stroke                  |
| <input type="radio"/> | C. Increased frequency of migraines                                  |
| <input type="radio"/> | D. Migraine is an independent risk factor for venous thromboembolism |
| <input type="radio"/> | E. Increased severity of migraines                                   |

[Next question](#)

### Migraine: pregnancy, contraception and other hormonal factors

SIGN produced guidelines in 2008 on the management of migraine, the following is selected highlights:

#### Migraine during pregnancy

- paracetamol 1g is first-line
- aspirin 300mg or ibuprofen 400mg can be used second-line in the first and second trimester

#### Migraine and the combined oral contraceptive (COC) pill

- if patients have migraine with aura then the COC is absolutely contraindicated due to an increased risk of stroke (relative risk 8.72)

#### Migraine and menstruation

- many women find that the frequency and severity of migraines increase around the time of menstruation
- SIGN recommends that women are treated with mefenamic acid or a combination of aspirin, paracetamol and caffeine. Triptans are also recommended in the acute situation

#### Migraine and hormone replacement therapy (HRT)

- safe to prescribe HRT for patients with a history of migraine but it may make migraines worse

Which one of the following statements regarding absence seizures is incorrect?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Typical age of onset of 3-10 years old                      |
| <input type="radio"/> | B. Sodium valproate and ethosuximide are first-line treatments |
| <input type="radio"/> | C. Seizures may be provoked by a child holding their breath    |
| <input type="radio"/> | D. There is a good prognosis                                   |
| <input type="radio"/> | E. Characteristic EEG changes are seen                         |

Next question

Seizures are characteristically provoked by hyperventilation

### Absence seizures

Absence seizures (petit mal) are a form of generalised epilepsy that is mostly seen in children. The typical age of onset of 3-10 years old and girls are affected twice as commonly as boys

#### Features

- absences last a few seconds and are associated with a quick recovery
- seizures may be provoked by hyperventilation or stress
- the child is usually unaware of the seizure
- they may occur many times a day
- EEG: bilateral, symmetrical 3Hz spike and wave pattern

#### Management

- sodium valproate and ethosuximide are first-line treatment
- good prognosis - 90-95% become seizure free in adolescence

Which one of the following is least associated with Miller-Fisher syndrome?

- |                       |                         |
|-----------------------|-------------------------|
| <input type="radio"/> | A. Anti-GQ1b antibodies |
| <input type="radio"/> | B. Areflexia            |
| <input type="radio"/> | C. Ataxia               |
| <input type="radio"/> | D. Postural hypotension |
| <input type="radio"/> | E. Ophthalmoplegia      |

Next question

Postural hypotension due to autonomic involvement is not a feature of Miller Fisher syndrome, but may be seen in Guillain-Barre syndrome

### Guillain-Barre syndrome

Guillain-Barre syndrome describes an immune mediated demyelination of the peripheral nervous system often triggered by an infection (classically *Campylobacter jejuni*)

#### Pathogenesis

- cross reaction of antibodies with gangliosides in the peripheral nervous system
- correlation between anti-ganglioside antibody (e.g. anti-GM1) and clinical features has been demonstrated
- anti-GM1 antibodies in 25% of patients

#### Miller Fisher syndrome

- variant of Guillain-Barre syndrome
- associated with ophthalmoplegia, areflexia and ataxia. The eye muscles are typically affected first
- usually presents as a descending paralysis rather than ascending as seen in other forms of Guillain-Barre syndrome
- anti-GQ1b antibodies are present in 90% of cases

A 67-year-old man who has a history of type 2 diabetes mellitus and benign prostatic hypertrophy presents with burning pain in his feet. This has been present for the past few months and is getting gradually worse. He has tried taking duloxetine but unfortunately has received no benefit. Clinical examination is unremarkable other than diminished sensation to fine touch on both soles. What is the most suitable initial management?

<input type="radio"/>	A. Carbamazepine
<input type="radio"/>	B. Amitriptyline
<input type="radio"/>	C. Pregabalin
<input type="radio"/>	D. Fluoxetine
<input type="radio"/>	E. Gabapentin

[Next question](#)

Amitriptyline would normally be first choice but given his history of benign prostatic hyperplasia it is better to avoid amitriptyline due to the risk of urinary retention.

### Diabetic neuropathy

NICE updated it's guidance on the management of diabetic neuropathy in 2010:

- first-line: oral duloxetine. Oral amitriptyline if duloxetine is contraindicated.
- second-line treatment: if first-line treatment was with duloxetine, switch to amitriptyline or pregabalin, or combine with pregabalin. If first-line treatment was with amitriptyline, switch to or combine with pregabalin
- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

### Gastroparesis

- symptoms include erratic blood glucose control, bloating and vomiting
- management options include metoclopramide, domperidone or erythromycin (prokinetic agents)

A 49-year-old man is prescribed procyclidine for Parkinson's disease. What is the mechanism of action?

<input type="radio"/>	A. Antimuscarinic
<input type="radio"/>	B. Dopamine receptor agonist
<input type="radio"/>	C. Decarboxylase inhibitor
<input type="radio"/>	D. Dopamine receptor antagonist
<input type="radio"/>	E. Monoamine Oxidase-B inhibitor

Next question

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

## Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

## COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

## Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benzotropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Which one of the following features is least typically of motor neuron disease?

<input type="radio"/>	A. Fasciculation
<input type="radio"/>	B. Dysarthria
<input type="radio"/>	C. Increased muscle tone
<input type="radio"/>	D. Ataxia
<input type="radio"/>	E. Absent reflexes

Next question

Ataxia is not a feature of motor neuron disease.

### Motor neuron disease: features

Motor neuron disease is a neurological condition of unknown cause which can present with both upper and lower motor neuron signs. It rarely presents before 40 years and various patterns of disease are recognised including amyotrophic lateral sclerosis, progressive muscular atrophy and bulbar palsy

There are a number of clues which point towards a diagnosis of motor neuron disease:

- fasciculation
- absence of sensory signs/symptoms\*
- lower motor neuron signs in arms and upper motor neuron signs in legs
- wasting of the small hand muscles/tibialis anterior is common

Other features

- doesn't affect external ocular muscles
- no cerebellar signs
- abdominal reflexes are usually preserved and sphincter dysfunction if present is a late feature

The diagnosis of motor neuron disease is clinical, but nerve conduction studies will show normal motor conduction and can help exclude a neuropathy. Electromyography shows a reduced number of action potentials with an increased amplitude. MRI is usually performed to exclude the differential diagnosis of cervical cord compression and myelopathy

\*vague sensory symptoms may occur early in the disease (e.g. limb pain) but 'never' sensory signs



A 35-year-old man presents with progressive weakness of his hands. On examination you notice wasting of the small muscles of the hand. A diagnosis of syringomyelia is suspected. Which one of the following features would most support this diagnosis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Hyper-reflexia in the upper limbs              |
| <input type="radio"/> | B. Loss of vibration sensation in the hands       |
| <input type="radio"/> | C. Loss of temperature sensation in the hands     |
| <input type="radio"/> | D. Loss of light touch sensation in the hands     |
| <input type="radio"/> | E. Fasciculation of the small muscles of the hand |

[Next question](#)

Syringomyelia - spinothalamic sensory loss (pain and temperature)

## Syringomyelia

### Overview

- development of cavity (syrinx) within the spinal cord
- if extends into medulla then termed syringobulbia
- strongly associated with the Arnold-Chiari malformation

### Features

- maybe asymmetrical initially
- slowly progressives, possibly over years
- motor: wasting and weakness of arms
- sensory: spinothalamic sensory loss (pain and temperature)
- loss of reflexes, bilateral upgoing plantars
- also seen: Horner's syndrome

Each one of the following is associated with the development of chorea, except:

<input type="radio"/>	A. Sarcoidosis
<input type="radio"/>	B. Wilson's disease
<input type="radio"/>	C. Anti-phospholipid syndrome
<input type="radio"/>	D. Pregnancy
<input type="radio"/>	E. Rheumatic fever

Next question

## Chorea

Chorea describes involuntary, rapid, jerky movements which often move from one part of the body to another. Slower, sinuous movement of the limbs is termed athetosis. Chorea is caused by damage to the basal ganglia, especially the caudate nucleus.

### Causes of chorea

- Huntington's disease, Wilson's disease, ataxic telangiectasia
- SLE, anti-phospholipid syndrome
- rheumatic fever: Sydenham's chorea
- drugs: oral contraceptive pill, L-dopa, antipsychotics
- neuroacanthocytosis
- pregnancy: chorea gravidarum
- thyrotoxicosis
- polycythaemia rubra vera
- carbon monoxide poisoning
- cerebrovascular disease

A 34-year-old man presents with headache and blurred vision for a few weeks. Investigations reveal:

Prolactin	21,500 mu/l
CT brain	Large pituitary mass encroaching on the optic chiasm with evidence of midline shift

What is the most appropriate treatment?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Dopamine agonist                |
| <input type="radio"/> | B. Trans-cranial hypophysectomy    |
| <input type="radio"/> | C. Trans-sphenoidal hypophysectomy |
| <input type="radio"/> | D. Pituitary irradiation           |
| <input type="radio"/> | E. Somatostatin                    |

Next question

Prolactinoma management - medical therapy is almost always first-line

Prolactinomas are unusual as medical therapy is first line, even if visual field defects are present. The main indications for surgery are tumours resistant to dopamine agonists

### Pituitary tumours

Hormones secreted

- PRL - 35%
- no obvious hormone, 'non-functioning', 'chromophobe' - 30%
- GH - 20%
- PRL and GH - 7%
- ACTH - 7%
- others: TSH, LH, FSH - 1%

Which one of the following antibiotics is most likely to exacerbate myasthenia gravis?

<input type="radio"/>	A. Metronidazole
<input type="radio"/>	B. Ceftriaxone
<input type="radio"/>	C. Trimethoprim
<input type="radio"/>	D. Doxycycline
<input type="radio"/>	E. Gentamicin

Next question

### Myasthenia gravis: exacerbating factors

The most common exacerbating factor is exertion resulting in fatigability, which is the hallmark feature of myasthenia gravis . Symptoms become more marked during the day

The following drugs may exacerbate myasthenia:

- penicillamine
- quinidine, procainamide
- beta-blockers
- lithium
- phenytoin
- gentamicin

A 51-year-old man with a history of schizophrenia is reviewed. He has developed parkinsonism secondary to his antipsychotic medication. Which one of the following drugs is most useful in the management of tremor?

<input type="radio"/>	A. Apomorphine
<input type="radio"/>	B. Cabergoline
<input type="radio"/>	C. Selegiline
<input type="radio"/>	D. Amantadine
<input type="radio"/>	E. Benzhexol

[Next question](#)

Benzhexol is now more commonly referred to as trihexyphenidyl. It is now mainly used for drug-induced parkinsonism rather than idiopathic Parkinson's disease

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

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- used in established PD

#### Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benzotropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

Which one of the following is least associated with myotonic dystrophy?

- ☐ A. Dysphagia
- ☐ B. Aortic regurgitation
- ☐ C. Diabetes mellitus
- ☐ D. Testicular atrophy
- ☐ E. Learning difficulties

Next question

### Dystrophia myotonica - DM1

- distal weakness initially
- autosomal dominant
- diabetes
- dysarthria

## Myotonic dystrophy

Myotonic dystrophy (also called dystrophia myotonica) is an inherited myopathy with features developing at around 20-30 years old. It affects skeletal, cardiac and smooth muscle. There are two main types of myotonic dystrophy, DM1 and DM2.

### Genetics

- autosomal dominant
- a trinucleotide repeat disorder
- DM1 is caused by a CTG repeat at the end of the DMPK (Dystrophia Myotonica-Protein Kinase) gene on chromosome 19
- DM2 is caused by a repeat expansion of the ZNF9 gene on chromosome 3

The key differences are listed in table below:

DM1	DM2
- DMPK gene on chromosome 19 - Distal weakness more prominent	- ZNF9 gene on chromosome 3 - Proximal weakness more prominent - Severe congenital form not seen

## General features

- myotonic facies (long, 'haggard' appearance)
- frontal balding
- bilateral ptosis
- cataracts
- dysarthria

## Other features

- myotonia (tonic spasm of muscle)
- weakness of arms and legs (distal initially)
- mild mental impairment
- diabetes mellitus
- testicular atrophy
- cardiac involvement: heart block, cardiomyopathy
- dysphagia



A 50-year-old man develops chronic, severe pain after sustaining a brachial plexus injury as a result of motorbike accident. He has had no benefit from paracetamol or ibuprofen. Following recent NICE guidelines, what is the most appropriate medication to consider?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Amitriptyline or gabapentin    |
| <input type="radio"/> | B. Gabapentin or duloxetine       |
| <input type="radio"/> | C. Amitriptyline or carbamazepine |
| <input type="radio"/> | D. Amitriptyline or pregabalin    |
| <input type="radio"/> | E. Duloxetine or pregabalin       |

[Next question](#)

### Neuropathic pain

Neuropathic pain may be defined as pain which arises following damage or disruption of the nervous system. It is often difficult to treat and responds poorly to standard analgesia.

Examples include:

- diabetic neuropathy
- post-herpetic neuralgia
- trigeminal neuralgia
- prolapsed intervertebral disc

NICE issued guidance in 2010 on the management of neuropathic pain:

- first-line treatment\*: oral amitriptyline or pregabalin
- if satisfactory pain reduction is obtained with amitriptyline but the person cannot tolerate the adverse effects, consider oral imipramine or nortriptyline as an alternative
- second-line treatment: if first-line treatment was with amitriptyline, switch to or combine with pregabalin. If first-line treatment was with pregabalin, switch to or

combine with amitriptyline

- other options: pain management clinic, tramadol (not other strong opioids), topical lidocaine for localised pain if patients unable to take oral medication

\*please note that for some specific conditions the guidance may vary. For example carbamazepine is used first-line for trigeminal neuralgia, duloxetine for diabetic neuropathy

### Question 192 of 204

A 24-year-old woman presents for advice. Over the past few months she has been having increasing problems with migraine around the time of menstruation. Her current migraine started around 24 hours ago and has not responded to a combination of paracetamol and aspirin. What is the most appropriate next step to relieve her headache?

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. Codeine        |
| <input type="radio"/> | B. Ergotamine     |
| <input type="radio"/> | C. Sumatriptan    |
| <input type="radio"/> | D. Venlafaxine    |
| <input type="radio"/> | E. Norethisterone |

[Next question](#)

Oral mefenamic acid would also be a suitable alternative.

### Migraine: pregnancy, contraception and other hormonal factors

SIGN produced guidelines in 2008 on the management of migraine, the following is selected highlights:

#### Migraine during pregnancy

- paracetamol 1g is first-line
- aspirin 300mg or ibuprofen 400mg can be used second-line in the first and second trimester

#### Migraine and the combined oral contraceptive (COC) pill

- if patients have migraine with aura then the COC is absolutely contraindicated due to an increased risk of stroke (relative risk 8.72)

#### Migraine and menstruation

- many women find that the frequency and severity of migraines increase around the time of menstruation
- SIGN recommends that women are treated with mefenamic acid or a combination of aspirin, paracetamol and caffeine. Triptans are also recommended in the acute situation

#### Migraine and hormone replacement therapy (HRT)

- safe to prescribe HRT for patients with a history of migraine but it may make migraines worse

A 71-year-old man is reviewed following an ischaemic stroke. He is known to be intolerant of clopidogrel. What is the most appropriate therapy to help reduce his chance of having a further stroke?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Aspirin + dipyridamole. Stop dipyridamole after 2 years |
| <input type="radio"/> | B. Dipyridamole. Stop dipyridamole after 2 years           |
| <input type="radio"/> | C. Aspirin lifelong  |
| <input type="radio"/> | D. Warfarin  |
| <input type="radio"/> | E. Aspirin + dipyridamole lifelong                         |

Next question

Please see the 2010 NICE guidelines for more details. The 2-year limit has now been removed.

### Stroke: management

The Royal College of Physicians (RCP) published guidelines on the diagnosis and management of patients following a stroke in 2004. NICE also issued stroke guidelines in 2008, although they modified their guidance with respect to antiplatelet therapy in 2010.

Selected points relating to the management of acute stroke include:

- blood glucose, hydration, oxygen saturation and temperature should be maintained within normal limits
- blood pressure should not be lowered in the acute phase unless there are complications e.g. Hypertensive encephalopathy\*
- aspirin 300mg orally or rectally should be given as soon as possible if a haemorrhagic stroke has been excluded
- with regards to atrial fibrillation, the RCP state: 'anticoagulants should not be started until brain imaging has excluded haemorrhage, and usually not until 14 days have passed from the onset of an ischaemic stroke'
- if the cholesterol is > 3.5 mmol/l patients should be commenced on a statin. Many physicians will delay treatment until after at least 48 hours due to the risk of haemorrhagic transformation

### Thrombolysis

Thrombolysis should only be given if:

- it is administered within 3 hours\*\* of onset of stroke symptoms (unless as part of a clinical trial)
- haemorrhage has been definitively excluded (i.e. Imaging has been performed)

Alteplase is currently recommended by NICE

### Secondary prevention

NICE also published a technology appraisal in 2010 on the use of clopidogrel and dipyridamole

Recommendations from NICE include:

- clopidogrel is now recommended by NICE ahead of combination use of aspirin plus modified release (MR) dipyridamole in people who have had an ischaemic stroke
- aspirin plus MR dipyridamole is now recommended after an ischaemic stroke only if clopidogrel is contraindicated or not tolerated, but treatment is no longer limited to 2 years' duration
- MR dipyridamole alone is recommended after an ischaemic stroke only if aspirin or clopidogrel are contraindicated or not tolerated, again with no limit on duration of treatment

With regards to carotid artery endarterectomy:

- recommend if patient has suffered stroke or TIA in the carotid territory and are not severely disabled
- should only be considered if carotid stenosis > 70% according ECST\*\*\* criteria or > 50% according to NASCET\*\*\*\* criteria

\*the 2009 Controlling hypertension and hypotension immediately post-stroke (CHHIPS) trial may change thinking on this but guidelines have yet to change to reflect this

\*\*SIGN recommend a window of 4.5 hours

\*\*\*European Carotid Surgery Trialists' Collaborative Group

\*\*\*\*North American Symptomatic Carotid Endarterectomy Trial

Antiepileptic medication is known to increase the risk of congenital defects. Which one of the following medications is thought to be associated with the lowest risk?

<input type="radio"/>	A. Levetiracetam
<input type="radio"/>	B. Sodium valproate
<input type="radio"/>	C. Phenytoin
<input type="radio"/>	D. Carbamazepine
<input type="radio"/>	E. Gabapentin

[Next question](#)

### Epilepsy: pregnancy and breast feeding

The risks of uncontrolled epilepsy during pregnancy generally outweigh the risks of medication to the fetus. All women thinking about becoming pregnant should be advised to take folic acid 5mg per day well before pregnancy to minimise the risk of neural tube defects. Around 1-2% of newborns born to non-epileptic mothers have congenital defects. This rises to 3-4% if the mother takes antiepileptic medication.

#### Other points

- aim for monotherapy
- there is no indication to monitor antiepileptic drug levels
- sodium valproate: associated with neural tube defects
- carbamazepine: often considered the least teratogenic of the older antiepileptics
- phenytoin: associated with cleft palate
- lamotrigine: studies to date suggest the rate of congenital malformations may be low. The dose of lamotrigine may need to be increased in pregnancy

Breast feeding is generally considered safe for mothers taking antiepileptics with the possible exception of the barbiturates

It is advised that pregnant women taking phenytoin are given vitamin K in the last month of pregnancy to prevent clotting disorders in the newborn

You review a 65-year-old man who is currently taking antipsychotic medication. His carers have noticed that his movements have been very slow over the past few weeks. Which one of the following would suggest a diagnosis of Parkinson's disease rather than drug-induced parkinsonism?

<input type="radio"/>	A. Rigidity
<input type="radio"/>	B. Masked face
<input type="radio"/>	C. Bilateral symptoms
<input type="radio"/>	D. Flexed posture
<input type="radio"/>	E. Restlessness of arms and legs

[Next question](#)

Rigidity and rest tremor are uncommon in drug-induced parkinsonism. Masked face and flexed posture can be seen in both conditions. Bilateral symptoms are more common in drug-induced parkinsonism. Restlessness of arms and legs (akathisia) is a common side-effect of antipsychotics.

### Parkinson's disease: features

Parkinson's disease is a progressive neurodegenerative condition caused by degeneration of dopaminergic neurons in the substantia nigra.. This results in a classic triad of features: bradykinesia, tremor and rigidity. The symptoms of Parkinson's disease are characteristically asymmetrical

#### Bradykinesia

- poverty of movement also seen: mask-like facies
- difficulty in initiating movement

#### Tremor

- most marked at rest, 3-5 Hz
- typically 'pill-rolling'

#### Rigidity

- lead pipe
- cogwheel: due to superimposed tremor

#### Other characteristic features

- flexed posture
- short, shuffling steps

- micrographia
- drooling of saliva
- psychiatric features: depression is the most common feature (affects about 40%); dementia, psychosis and sleep disturbances may also occur
- impaired olfaction
- REM sleep behaviour disorder

**Drug-induced parkinsonism** has slightly different features to Parkinson's disease:

- motor symptoms are generally rapid onset and bilateral
- rigidity and rest tremor are uncommon

Each one of the following drugs may be used to prevent migraine attacks, except:

<input type="radio"/>	A. Pizotifen
<input type="radio"/>	B. Amitriptyline
<input type="radio"/>	C. Propranolol
<input type="radio"/>	D. Methysergide
<input type="radio"/>	E. Sumatriptan

Next question

### Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. NICE produced guidelines in 2012 on the management of headache, including migraines.

#### Acute treatment

- first-line: offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol
- for young people aged 12-17 years consider a nasal triptan in preference to an oral triptan
- if the above measures are not effective or not tolerated offer a non-oral preparation of metoclopramide\* or prochlorperazine and consider adding a non-oral NSAID or triptan

#### Prophylaxis

- prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients.
- NICE advise either topiramate or propranolol 'according to the person's preference, comorbidities and risk of adverse events'. Propranolol should be used in preference to topiramate in women of child bearing age as it may be teratogenic and it can reduce the effectiveness of hormonal contraceptives
- if these measures fail NICE recommend 'a course of up to 10 sessions of acupuncture over 5-8 weeks' or gabapentin
- NICE recommend: 'Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people'
- for women with predictable menstrual migraine treatment NICE recommend either frovatriptan (2.5 mg twice a day) or zolmitriptan (2.5 mg twice or three times a day) as a type of 'mini-prophylaxis'
- pizotifen is no longer recommend. Adverse effects such as weight gain & drowsiness are common

\*caution should be exercised with young patients as acute dystonic reactions may develop



Each of the following are causes of peripheral neuropathy. Which one is associated with predominately sensory loss?

<input type="radio"/>	A. Diphtheria
<input type="radio"/>	B. Hereditary sensorimotor neuropathies
<input type="radio"/>	C. Porphyria
<input type="radio"/>	D. Lead poisoning
<input type="radio"/>	E. Uraemia

[Next question](#)

## Peripheral neuropathy

Peripheral neuropathy may be divided into conditions which predominately cause a motor or sensory loss

Predominately motor loss

- Guillain-Barre syndrome
- porphyria
- lead poisoning
- hereditary sensorimotor neuropathies (HSMN) - Charcot-Marie-Tooth
- chronic inflammatory demyelinating polyneuropathy (CIDP)
- diphtheria

Predominately sensory loss

- diabetes
- uraemia
- leprosy
- alcoholism
- vitamin B12 deficiency
- amyloidosis

Alcoholic neuropathy

- secondary to both direct toxic effects and reduced absorption of B vitamins
- sensory symptoms typically present prior to motor symptoms

Vitamin B12 deficiency

- subacute combined degeneration of spinal cord
- dorsal column usually affected first (joint position, vibration) prior to distal paraesthesia

Which one of the following causes of peripheral neuropathy is most associated with an axonal, rather than demyelinating, pathology?

<input type="radio"/>	A. Paraprotein neuropathy
<input type="radio"/>	B. Guillain-Barre syndrome
<input type="radio"/>	C. Hereditary sensorimotor neuropathies (HSMN) type I
<input type="radio"/>	D. Amiodarone
<input type="radio"/>	E. Vasculitis

[Next question](#)

The other causes are associated with a demyelinating pathology

### Peripheral neuropathy: demyelinating vs. axonal

Demyelinating pathology

- Guillain-Barre syndrome
- chronic inflammatory demyelinating polyneuropathy (CIDP)
- amiodarone
- hereditary sensorimotor neuropathies (HSMN) type I
- paraprotein neuropathy

Axonal pathology

- alcohol
- diabetes mellitus\*
- vasculitis
- vitamin B12 deficiency\*
- hereditary sensorimotor neuropathies (HSMN) type II

\* may also cause a demyelinating picture

A 67-year-old woman comes for review with her husband. Her husband complains that she is constantly getting up from bed at night and pacing around the bedroom. She complains of 'antsy' legs and a 'horrible, creeping sensation'. Her symptoms generally come on in the evening and are only relieved by moving round. Given the likely diagnosis, what is the most appropriate treatment?

- ☐ A. Ropinirole
- ☐ B. Carbamazepine
- ☐ C. Amitriptyline
- ☐ D. Citalopram
- ☐ E. Quinine

[Next question](#)

Restless leg syndrome - management includes dopamine agonists such as ropinirole

## Restless legs syndrome

Restless legs syndrome (RLS) is a syndrome of spontaneous, continuous lower limb movements that may be associated with paraesthesia. It is extremely common, affecting between 2-10% of the general population. Males and females are equally affected and a family history may be present

### Clinical features

- uncontrollable urge to move legs (akathisia). Symptoms initially occur at night but as condition progresses may occur during the day. Symptoms are worse at rest
- paraesthesias e.g. 'crawling' or 'throbbing' sensations
- movements during sleep may be noted by the partner - periodic limb movements of sleep (PLMS)

### Causes and associations

- there is a positive family history in 50% of patients with idiopathic RLS
- iron deficiency anaemia
- uraemia
- diabetes mellitus
- pregnancy

The diagnosis is clinical although bloods to exclude iron deficiency anaemia may be appropriate

## Management

- simple measures: walking, stretching, massaging affected limbs
- treat any iron deficiency
- dopamine agonists are first-line treatment (e.g. Pramipexole, ropinirole)
- benzodiazepines
- gabapentin

A 45-year-old female with a past medical history of asthma is diagnosed as having essential tremor. What is the most suitable management?

<input type="radio"/>	A. Amitriptyline
<input type="radio"/>	B. Propranolol
<input type="radio"/>	C. Sodium valproate
<input type="radio"/>	D. Carbamazepine
<input type="radio"/>	E. Primidone

[Next question](#)

Essential tremor is an AD condition that is made worse when arms are outstretched, made better by alcohol and propranolol

Propranolol is generally considered first-line in essential but given the history of asthma primidone should be used

### Essential tremor

Essential tremor (previously called benign essential tremor) is an autosomal dominant condition which usually affects both upper limbs

#### Features

- postural tremor: worse if arms outstretched
- improved by alcohol and rest
- most common cause of titubation (head tremor)

#### Management

- propranolol is first-line
- primidone is sometimes used

Which one of the following antibodies is associated with ocular opsoclonus-myoclonus in patients with breast cancer?

<input type="radio"/>	A. Anti-Hu
<input type="radio"/>	B. Anti-La
<input type="radio"/>	C. Anti-GAD
<input type="radio"/>	D. Anti-Yo
<input type="radio"/>	E. Anti-Ri

[Next question](#)

### Paraneoplastic syndromes affecting nervous system

#### Lambert-Eaton myasthenic syndrome

- associated with small cell lung cancer (also breast and ovarian)
- antibody directed against pre-synaptic voltage gated calcium channel in the peripheral nervous system
- can also occur independently as autoimmune disorder

#### Anti-Hu

- associated with small cell lung carcinoma and neuroblastomas
- sensory neuropathy - may be painful
- cerebellar syndrome
- encephalomyelitis

#### Anti-Yo

- associated with ovarian and breast cancer
- cerebellar syndrome

#### Anti-GAD antibody

- associated with breast, colorectal and small cell lung carcinoma
- stiff person's syndrome or diffuse hypertonia

#### Anti-Ri

- associated with breast and small cell lung carcinoma
- ocular opsoclonus-myoclonus

A 24-year-old woman who is 14 weeks pregnant presents with a severe migraine. She has a long history of migraine and stopped propranolol prophylaxis when she found out she was pregnant. Unfortunately the headache has not responded to paracetamol 1g. What is the most appropriate next step?

<input type="radio"/>	A. Ergotamine
<input type="radio"/>	B. Nasal zolmitriptan
<input type="radio"/>	C. Ibuprofen 400mg
<input type="radio"/>	D. Almotriptan 12.5mg
<input type="radio"/>	E. Codeine 30mg

[Next question](#)

### Migraine: pregnancy, contraception and other hormonal factors

SIGN produced guidelines in 2008 on the management of migraine, the following is selected highlights:

#### Migraine during pregnancy

- paracetamol 1g is first-line
- aspirin 300mg or ibuprofen 400mg can be used second-line in the first and second trimester

#### Migraine and the combined oral contraceptive (COC) pill

- if patients have migraine with aura then the COC is absolutely contraindicated due to an increased risk of stroke (relative risk 8.72)

#### Migraine and menstruation

- many women find that the frequency and severity of migraines increase around the time of menstruation
- SIGN recommends that women are treated with mefenamic acid or a combination of aspirin, paracetamol and caffeine. Triptans are also recommended in the acute situation

#### Migraine and hormone replacement therapy (HRT)

- safe to prescribe HRT for patients with a history of migraine but it may make migraines worse

Which one of the following statements regarding Meniere's disease is correct?

<input type="radio"/>	A. More common in patients from the Indian Subcontinent
<input type="radio"/>	B. Symptoms resolve in the majority of patients after 6-12 months
<input type="radio"/>	C. It is very rare that patients develop permanent hearing loss
<input type="radio"/>	D. More common in children
<input type="radio"/>	E. Approximately equal incidence in males and females

Next question

### Meniere's disease

Meniere's disease is a disorder of the inner ear of unknown cause. It is characterised by excessive pressure and progressive dilation of the endolymphatic system. It is more common in middle-aged adults but may be seen at any age. Meniere's disease has a similar prevalence in both men and women.

#### Features

- recurrent episodes of vertigo, tinnitus and hearing loss (sensorineural). Vertigo is usually the prominent symptom
- a sensation of aural fullness or pressure is now recognised as being common
- other features include nystagmus and a positive Romberg test
- episodes last minutes to hours
- typically symptoms are unilateral but bilateral symptoms may develop after a number of years

#### Natural history

- symptoms resolve in the majority of patients after 5-10 years
- some patients may be left with hearing loss
- psychological distress is common

#### Management

- ENT assessment is required to confirm the diagnosis
- patients should inform the DVLA. The current advice is to cease driving until satisfactory control of symptoms is achieved
- acute attacks: buccal or intramuscular prochlorperazine. Admission is sometimes required
- prevention: betahistine may be of benefit



### Question 204 of 204

A 39-year-old man is diagnosed as having cluster headaches. He has received subcutaneous sumatriptan on two occasions but would like to start medication to help prevent further attacks. Of the following options, which one is the most suitable treatment?

<input type="radio"/>	A. Atenolol
<input type="radio"/>	B. Amitriptyline
<input type="radio"/>	C. Sodium valproate
<input type="radio"/>	D. Verapamil
<input type="radio"/>	E. Gabapentin

### Cluster headache

Cluster headaches\* are more common in men (5:1) and smokers

#### Features

- pain typical occurs once or twice a day, each episode lasting 15 mins - 2 hours
- clusters typically last 4-12 weeks
- intense pain around one eye (recurrent attacks 'always' affect same side)
- patient is restless during an attack
- accompanied by redness, lacrimation, lid swelling
- nasal stuffiness
- miosis and ptosis in a minority

#### Management

- acute: 100% oxygen, subcutaneous sumatriptan, nasal lidocaine
- prophylaxis: verapamil, prednisolone
- consider specialist referral

\*some neurologists use the term trigeminal autonomic cephalgia to group a number of conditions including cluster headache, paroxysmal hemicrania and short-lived unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). It is recommended such patients are referred for specialist assessment as specific treatment may be required, for example it is known paroxysmal hemicrania responds very well to indomethacin

**Question 1 of 167**

Next

A 34-year-old man with a past history of HIV infection presents to the Emergency Department with watery diarrhoea. Cryptosporidium infection is confirmed on ZN staining. What is the most suitable management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Metronidazole                            |
| <input type="radio"/> | B. Sulfadiazine + pyrimethamine             |
| <input type="radio"/> | C. Supportive therapy                       |
| <input type="radio"/> | D. Rifampicin + ethambutol + clarithromycin |
| <input type="radio"/> | E. Co-trimoxazole                           |

Next question

Supportive therapy is the mainstay of treatment in *Cryptosporidium* diarrhoea

**HIV: diarrhoea**

Diarrhoea is common in patients with HIV. This may be due to the effects of the virus itself (HIV enteritis) or opportunistic infections

Possible causes

- *Cryptosporidium* + other protozoa (most common)
- Cytomegalovirus
- *Mycobacterium avium intracellulare*
- *Giardia*

*Cryptosporidium* is the most common infective cause of diarrhoea in HIV patients. It is an intracellular protozoa and has an incubation period of 7 days. Presentation is very variable, ranging from mild to severe diarrhoea. A modified Ziehl-Neelsen stain (acid-fast stain) of the stool may reveal the characteristic red cysts of *Cryptosporidium*. Treatment is difficult, with the mainstay of management being supportive therapy\*

*Mycobacterium avium intracellulare* is an atypical mycobacteria seen with the CD4 count is below 50. Typical features include fever, sweats, abdominal pain and diarrhoea. There may be hepatomegaly and deranged LFTs. Diagnosis is made by blood cultures and bone marrow examination. Management is with rifabutin, ethambutol and clarithromycin

\*nitazoxanide is licensed in the US for immunocompetent patients

Which one of the following is a live attenuated vaccine?

<input type="radio"/>	A. Yellow fever
<input type="radio"/>	B. Rabies
<input type="radio"/>	C. Pertussis
<input type="radio"/>	D. Diphtheria
<input type="radio"/>	E. Tetanus

Next question

#### Live attenuated vaccines

- BCG
- MMR
- oral polio
- yellow fever
- oral typhoid

### Vaccinations

It is important to be aware of vaccines which are of the live-attenuated type as these may pose a risk to immunocompromised patients. The main types of vaccine are as follows:

#### Live attenuated

- BCG
- measles, mumps, rubella (MMR)
- oral polio
- yellow fever
- oral typhoid\*

#### Inactivated preparations

- rabies
- influenza

#### Detoxified exotoxins

- tetanus

Extracts of the organism/virus (sometimes termed fragment)\*\*

- diphtheria
- pertussis ('acellular' vaccine)
- hepatitis B
- meningococcus, pneumococcus, haemophilus

## Notes

- influenza: different types are available, including whole inactivated virus, split virion (virus particles disrupted by detergent treatment) and sub-unit (mainly haemagglutinin and neuraminidase)
- cholera: contains inactivated Inaba and Ogawa strains of *Vibrio cholerae* together with recombinant B-subunit of the cholera toxin
- hepatitis B: contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology

\*whole cell typhoid vaccine is no longer used in the UK

\*\*may also be produced using recombinant DNA technology

A 22-year-old woman who is an immigrant from Malawi presents for review as she thinks she is pregnant. This is confirmed with a positive pregnancy test. She is known to be HIV positive. Which one of the following should not be part of the management plan to ensure an optimal outcome?

<input type="radio"/>	A. Oral zidovudine for the newborn until 6 weeks of age
<input type="radio"/>	B. Maternal antiretroviral therapy
<input type="radio"/>	C. Encourage breast feeding
<input type="radio"/>	D. Intrapartum zidovudine infusion
<input type="radio"/>	E. Elective caesarean section

[Next question](#)

The 2008 BHIVA guidelines suggest vaginal delivery may be an option for women on HAART who have an undetectable viral load but whether this will translate into clinical practice remains to be seen

### HIV and pregnancy

With the increased incidence of HIV infection amongst the heterosexual population there are an increasing number of HIV positive women giving birth in the UK. In London the incidence may be as high as 0.4% of pregnant women. The aim of treating HIV positive women during pregnancy is to minimise harm to both the mother and fetus, and to reduce the chance of vertical transmission.

Factors which reduce vertical transmission (from 25-30% to 2%)

- maternal antiretroviral therapy
- mode of delivery (caesarean section)
- neonatal antiretroviral therapy
- infant feeding (bottle feeding)

### Screening

- NICE guidelines recommend offering HIV screening to all pregnant women

### Antiretroviral therapy

- all pregnant women should be offered antiretroviral therapy regardless of whether they were taking it previously
- if women are not currently taking antiretroviral therapy the RCOG recommend that it is commenced between 28 and 32 weeks of gestation and should be continued intrapartum. BHIVA recommend that antiretroviral therapy may be started at an earlier gestation depending upon the individual situation

## Mode of delivery

- elective caesarean section\*
- a zidovudine infusion should be started four hours before beginning the caesarean section

## Neonatal antiretroviral therapy

- zidovudine is usually administered orally to the neonate for four to six weeks

## Infant feeding

- in the UK all women should be advised not to breast feed

\*the 2008 BHIVA guidelines suggest vaginal delivery may be an option for women on HAART who have an undetectable viral load but whether this will translate into clinical practice remains to be seen

#### Question 4 of 167

Next

A 34-year-old man from Zimbabwe is admitted with abdominal pain to the Emergency Department. An abdominal x-ray reveals urinary bladder calcification. What is the most likely cause?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. <i>Schistosoma mansoni</i>     |
| <input type="radio"/> | B. Sarcoidosis                    |
| <input type="radio"/> | C. Leishmaniasis                  |
| <input type="radio"/> | D. Tuberculosis                   |
| <input type="radio"/> | E. <i>Schistosoma haematobium</i> |

Next question

*Schistosoma haematobium* causes **haematuria**

Schistosomiasis is the most common cause of bladder calcification worldwide

#### Schistosomiasis

Schistosomiasis, or bilharzia, is a parasitic flatworm infection. The following types of schistosomiasis are recognised:

- *Schistosoma mansoni* and *Schistosoma intercalatum*: intestinal schistosomiasis
- *Schistosoma haematobium*: urinary schistosomiasis

#### *Schistosoma haematobium*

This typically presents as a 'swimmer's itch' in patients who have recently returned from Africa. *Schistosoma haematobium* is a risk factor for squamous cell bladder cancer

#### Features

- frequency
- haematuria
- bladder calcification

#### Management

- single oral dose of praziquantel

Which one of the following best describes the action of aciclovir?

<input type="radio"/>	A. Inhibits uncoating of virus in the cell
<input type="radio"/>	B. Inhibits DNA polymerase
<input type="radio"/>	C. Interferes with the capping of viral mRNA
<input type="radio"/>	D. Inhibits RNA polymerase
<input type="radio"/>	E. Protease inhibitor

Next question

## Antiviral agents

### Aciclovir

- aciclovir is phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase

### Ribavirin

- effective against a range of DNA and RNA viruses
- interferes with the capping of viral mRNA

### Interferons

- inhibit synthesis of mRNA, translation of viral proteins, viral assembly and release

### Amantadine

- used to treat influenza
- inhibits uncoating of virus in cell

## Anti-retroviral agent used in HIV

### Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine

### Protease inhibitors (PI)

- inhibits a protease needed to make the virus able to survive outside the cell
- examples: indinavir, nelfinavir, ritonavir, saquinavir

### Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz



**Question 6 of 167**

Next

A 24-year-old woman who is 18 weeks pregnant presents to the Emergency Department. Earlier on in the morning she came into contact with a child who has chickenpox. She is unsure if she had the condition herself as a child. What is the most appropriate action?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Advise her to present within 24 hours of the rash developing for consideration of IV aciclovir |
| <input type="radio"/> | B. Reassure her that there is no risk of fetal complications at this point in pregnancy           |
| <input type="radio"/> | C. Give varicella immunoglobulin  |
| <input type="radio"/> | D. Check varicella antibodies   |
| <input type="radio"/> | E. Prescribe oral aciclovir   |

Next question

Chickenpox exposure in pregnancy - first step is to check antibodies

If there is any doubt about the mother previously having chickenpox maternal blood should be checked for varicella antibodies

**Chickenpox exposure in pregnancy**

Chickenpox is caused by primary infection with varicella zoster virus. Shingles is reactivation of dormant virus in dorsal root ganglion. In pregnancy there is a risk to both the mother and also the fetus, a syndrome now termed fetal varicella syndrome

**Fetal varicella syndrome (FVS)**

- risk of FVS following maternal varicella exposure is around 1% if occurs before 20 weeks gestation
- studies have shown a very small number of cases occurring between 20-28 weeks gestation and none following 28 weeks
- features of FVS include skin scarring, eye defects (microphthalmia), limb hypoplasia, microcephaly and learning disabilities

**Management of chickenpox exposure**

- if there is any doubt about the mother previously having chickenpox maternal blood should be checked for varicella antibodies
- if the pregnant woman is not immune to varicella she should be given varicella zoster immunoglobulin (VZIG) as soon as possible. RCOG and Greenbook guidelines suggest VZIG is effective up to 10 days post exposure
- consensus guidelines suggest oral aciclovir should be given if pregnant women with chickenpox present within 24 hours of onset of the rash

**Question 7 of 167**

Next

A 19-year-old man presents with dysuria associated with a watery discharge from his urethral meatus. A urethral swab shows non-specific urethritis and urine is sent for *Chlamydia*/gonococcus. What is the most appropriate antibiotic to use?

<input type="radio"/>	A. Erythromycin
<input type="radio"/>	B. Ciprofloxacin
<input type="radio"/>	C. Metronidazole
<input type="radio"/>	D. Cefixime
<input type="radio"/>	E. Azithromycin

Next question

*Chlamydia* - treat with azithromycin or doxycycline

Gonorrhoea would be demonstrated by the presence of Gram negative diplococci on the swab. As the swab showed non-specific urethritis a diagnosis of *Chlamydia* is most likely.

The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline.

***Chlamydia***

*Chlamydia* is the most prevalent sexually transmitted infection in the UK and is caused by *Chlamydia trachomatis*, an obligate intracellular pathogen. Approximately 1 in 10 young women in the UK have *Chlamydia*. The incubation period is around 7-21 days, although it should be remembered a large percentage of cases are asymptomatic

**Features**

- asymptomatic in around 70% of women and 50% of men
- women: cervicitis (discharge, bleeding), dysuria
- men: urethral discharge, dysuria

**Potential complications**

- epididymitis
- pelvic inflammatory disease
- endometritis
- increased incidence of ectopic pregnancies
- infertility
- reactive arthritis

- perihepatitis (Fitz-Hugh-Curtis syndrome)

## Investigation

- traditional cell culture is no longer widely used
- nuclear acid amplification tests (NAATs) are now rapidly emerging as the investigation of choice
- urine (first void urine sample), vulvovaginal swab or cervical swab may be tested using the NAAT technique

## Screening

- in England the National *Chlamydia* Screening Programme is open to all men and women aged 15-24 years
- the 2009 SIGN guidelines support this approach, suggesting screening all sexually active patients aged 15-24 years
- relies heavily on opportunistic testing

## Management

- doxycycline (7 day course) or azithromycin (single dose). The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline
- if pregnant then erythromycin or amoxicillin may be used. The SIGN guidelines suggest considering azithromycin 'following discussion of the balance of benefits and risks with the patient'
- patients diagnosed with *Chlamydia* should be offered a choice of provider for initial partner notification - either trained practice nurses with support from GUM, or referral to GUM
- for men with symptomatic infection all partners from the four weeks prior to the onset of symptoms should be contacted
- for women and asymptomatic men all partners from the last six months or the most recent sexual partner should be contacted
- contacts of confirmed *Chlamydia* cases should be offered treatment prior to the results of their investigations being known (treat then test)

### Question 8 of 167

Next

A 54-year-old female is admitted with a severe pneumonia following a holiday in Turkey. Bloods reveal both hyponatraemia and deranged liver function tests. A chest x-ray shows patchy alveolar infiltrates with consolidation in the right lower lobe. Which one of the following investigations is most likely to confirm the probable diagnosis?

<input type="radio"/>	A. Sputum culture
<input type="radio"/>	B. Urinary antigen
<input type="radio"/>	C. Blood cultures
<input type="radio"/>	D. Bone marrow aspirate
<input type="radio"/>	E. Lumbar puncture

Next question

**Legionella pneumophila** is best diagnosed by the **urinary antigen** test

### Legionella

Legionnaire's disease is caused by the intracellular bacterium *Legionella pneumophila*. It typically colonizes water tanks and hence questions may hint at air-conditioning systems or foreign holidays. Person-to-person transmission is not seen

#### Features

- flu-like symptoms
- dry cough
- relative bradycardia
- confusion
- lymphopenia
- hyponatraemia
- deranged LFTs

#### Diagnosis

- urinary antigen

#### Management

- treat with erythromycin

A 28-year-old man is admitted to the Emergency Department with dyspnoea and fever. Two days ago he developed an itchy, vesicular rash after coming into contact with a child who had chickenpox. On examination his temperature is 38.6°C, respiratory rate 24 / min, pulse 120 / min and blood pressure 135/68 mmHg. Oxygen saturations are 95% on room air. Examination of chest reveals only occasional fine crackles bilaterally. What is the most important intervention?

<input type="radio"/>	A. Elective intubation within the next 2 hours
<input type="radio"/>	B. Prednisolone
<input type="radio"/>	C. Varicella zoster immunoglobulin
<input type="radio"/>	D. IV aciclovir
<input type="radio"/>	E. Paracetamol

[Next question](#)

Varicella pneumonia is the most common and serious complication of chickenpox infection in adults. Auscultation of the chest is often unremarkable. Varicella zoster immunoglobulin is used for the prevention of varicella in at-risk groups (e.g. Immunocompromised, pregnant women), rather than for treatment

### Chickenpox

Chickenpox is caused by primary infection with varicella zoster virus. Shingles is reactivation of dormant virus in dorsal root ganglion

Chickenpox is highly infectious

- spread via the respiratory route
- can be caught from someone with shingles
- infectivity = 4 days before rash, until 5 days after the rash first appeared\*
- incubation period = 10-21 days

Clinical features (tend to be more severe in older children/adults)

- fever initially
- itchy, rash starting on head/trunk before spreading. Initially macular then papular then vesicular
- systemic upset is usually mild

Management is supportive

- keep cool, trim nails
- calamine lotion

- school exclusion: current HPA advice is 5 days from start of skin eruption. They also state 'Traditionally children have been excluded until all lesions are crusted. However, transmission has never been reported beyond the fifth day of the rash.'
- immunocompromised patients and newborns with peripartum exposure should receive varicella zoster immunoglobulin (VZIG). If chickenpox develops then IV aciclovir should be considered

A common complication is secondary bacterial infection of the lesions. Rare complications include

- pneumonia
- encephalitis (cerebellar involvement may be seen)
- disseminated haemorrhagic chickenpox
- arthritis, nephritis and pancreatitis may very rarely be seen

\*it was traditionally taught that patients were infective until all lesions had scabbed over

A 17-year-old female presents for review. Four days ago she presented to her doctor with a severe sore throat, lethargy and headache. Her doctor prescribed a course of amoxicillin to treat an upper respiratory tract infection. Two days ago she developed a widespread, pruritic maculopapular rash. Her original symptoms have also not improved. What is the most likely diagnosis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Infectious mononucleosis                           |
| <input type="radio"/> | B. Kawasaki disease                                   |
| <input type="radio"/> | C. Penicillin allergy                                 |
| <input type="radio"/> | D. HIV seroconversion                                 |
| <input type="radio"/> | E. Beta-lactamase producing streptococcal sore throat |

[Next question](#)

URTI symptoms + amoxicillin --> rash ?glandular fever

A rash develops in around 99% of patients who take amoxicillin whilst they have infectious mononucleosis. Her treatment should be supportive as detailed below.

### Infectious mononucleosis

Infectious mononucleosis (glandular fever) is caused by the Epstein-Barr virus (also known as human herpesvirus 4, HHV-4). It is most common in adolescents and young adults.

#### Features

- sore throat
- lymphadenopathy
- pyrexia
- malaise, anorexia, headache
- palatal petechiae
- splenomegaly - occurs in around 50% of patients and may rarely predispose to splenic rupture
- hepatitis
- presence of 50% lymphocytes with at least 10% atypical lymphocytes
- haemolytic anaemia
- a maculopapular, pruritic rash develops in around 99% of patients who take ampicillin/amoxicillin whilst they have infectious mononucleosis

Management is supportive and includes:

- rest during the early stages, drink plenty of fluid, avoid alcohol
- simple analgesia for any aches or pains
- consensus guidance in the UK is to avoid playing contact sports for 8 weeks after having glandular fever to reduce the risk of splenic rupture

A 35-year-old homosexual man is referred to the local genitourinary clinic following the development of a solitary painless penile ulcer associated with painful inguinal lymphadenopathy. He has recently developed rectal pain and tenesmus. What is the most likely diagnosis?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Herpes simplex infection |
| <input type="radio"/> | B. Syphilis                 |
| <input type="radio"/> | C. Granuloma inguinale      |
| <input type="radio"/> | D. Chancroid                |
| <input type="radio"/> | E. Lymphogranuloma venereum |

[Next question](#)

#### Genital ulcers

- painful: herpes much more common than chancroid
- painless: syphilis more common than lymphogranuloma venereum + granuloma inguinale

Lymphogranuloma venereum usually involves three stages:

- 1 - small painless pustule which later forms an ulcer
- 2 - painful inguinal lymphadenopathy
- 3 - proctocolitis

#### STI: ulcers

Genital herpes is most often caused by the herpes simplex virus (HSV) type 2 (cold sores are usually due to HSV type 1). Primary attacks are often severe and associated with fever whilst subsequent attacks are generally less severe and localised to one site

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*. Infection is characterised by primary, secondary and tertiary stages. A painless ulcer (chancre) is seen in the primary stage. The incubation period= 9-90 days

Chancroid is a tropical disease caused by *Haemophilus ducreyi*. It causes painful genital ulcers associated with inguinal lymph node enlargement

Lymphogranuloma venereum is caused by *Chlamydia trachomatis*. Typically infection comprises of three stages

- stage 1: small painless pustule which later forms an ulcer



- stage 2: painful inguinal lymphadenopathy
- stage 3: proctocolitis

#### Other causes of genital ulcers

- Behcet's disease
- carcinoma
- granuloma inguinale: *Klebsiella granulomatis*\*

\*previously called *Calymmatobacterium granulomatis*

Which one of the following organisms causes erysipelas?

<input type="radio"/>	A. <i>Staphylococcus aureus</i>
<input type="radio"/>	B. <i>Streptococcus pneumoniae</i>
<input type="radio"/>	C. <i>Staphylococcus epidermidis</i>
<input type="radio"/>	D. <i>Streptococcus pyogenes</i>
<input type="radio"/>	E. <i>Streptococcus viridans</i>

Next question

## Streptococci

Streptococci are gram-positive cocci. They may be divided into alpha and beta haemolytic types

### Alpha haemolytic streptococci (partial haemolysis)

The most important alpha haemolytic *Streptococcus* is *Streptococcus pneumoniae* (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is *Streptococcus viridans*

### Beta haemolytic streptococci (complete haemolysis)

These can be subdivided into groups A-H. Only groups A, B & D are important in humans.

#### Group A

- most important organism is *Streptococcus pyogenes*
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

#### Group B

- *Streptococcus agalactiae* may lead to neonatal meningitis and septicaemia

#### Group D

- *Enterococcus*

**Question 13 of 167**

Next

A 39-year-old man is admitted to hospital with decompensated liver disease of unknown aetiology. As part of a liver screen the following results are obtained:

Anti-HBs	Positive
Anti-HBc	Negative
HBs antigen	Negative

Anti-HBs = Hepatitis B Surface Antibody; Anti-HBc = Hepatitis B Core Antibody; HBs antigen = Hepatitis B Surface Antigen

What is this man's hepatitis B status?

- ☐ A. Chronic hepatitis B - highly infectious
- ☐ B. Previous immunisation to hepatitis B
- ☐ C. Probable hepatitis D infection
- ☐ D. Acute hepatitis B infection
- ☐ E. Chronic hepatitis B - not infectious

Next question

**Hepatitis B serology**

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months. IgG anti-HBc persists
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

**Example results**

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

A 38-year-old man presents to the genitourinary clinic with multiple, painless genital ulcers. A diagnosis of granuloma inguinale is made. What is the causative organism?

<input type="radio"/>	A. <i>Klebsiella granulomatis</i>
<input type="radio"/>	B. <i>Chlamydia</i>
<input type="radio"/>	C. Herpes simplex virus
<input type="radio"/>	D. <i>Treponema pallidum</i>
<input type="radio"/>	E. <i>Haemophilus ducreyi</i>

[Next question](#)

### STI: ulcers

Genital herpes is most often caused by the herpes simplex virus (HSV) type 2 (cold sores are usually due to HSV type 1). Primary attacks are often severe and associated with fever whilst subsequent attacks are generally less severe and localised to one site

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Lymphogranuloma venereum is caused by *Chlamydia trachomatis*. Typically infection comprises of three stages

- stage 1: small painless pustule which later forms an ulcer
- stage 2: painful inguinal lymphadenopathy
- stage 3: proctocolitis

Other causes of genital ulcers

- Behcet's disease
- carcinoma
- granuloma inguinale: *Klebsiella granulomatis*\*

\*previously called *Calymmatobacterium granulomatis*

**Question 15 of 167**

Next

A 19-year-old man presents with an annular rash, pyrexia and polyarthralgia to an the Emergency Department. He has just returned from the New Forest and remembers being bitten by a tick. Given the likely diagnosis, what is the most appropriate antibiotic therapy?

<input type="radio"/>	A. Ciprofloxacin
<input type="radio"/>	B. Amoxicillin
<input type="radio"/>	C. Metronidazole
<input type="radio"/>	D. Doxycycline
<input type="radio"/>	E. Ceftriaxone

Next question

As he only has features of early disease, doxycycline is sufficient.

**Lyme disease**

Lyme disease is caused by the spirochaete *Borrelia burgdorferi* and is spread by ticks

**Features**

- early: erythema chronicum migrans + systemic features (fever, arthralgia)
- CVS: heart block, myocarditis
- neuro: cranial nerve palsies, meningitis

**Investigation**

- serology: antibodies to *Borrelia burgdorferi*

**Management**

- doxycycline if early disease
- ceftriaxone if disseminated disease
- Jarisch-Herxheimer reaction is sometimes seen after initiating therapy: fever, rash, tachycardia after first dose of antibiotic (more commonly seen in syphilis, another spirochaetal disease)

**Question 16 of 167**

Next

A 27-year-old male presents with malaise, pyrexia, lymphadenopathy and a maculopapular rash. The Monospot test is negative. Given a history of high-risk sexual behaviour you are asked to exclude a HIV seroconversion illness. What is the most appropriate investigation?

<input type="radio"/>	A. Antibodies to HIV-2
<input type="radio"/>	B. gp120 polymerase chain reaction
<input type="radio"/>	C. p24 antigen test
<input type="radio"/>	D. CCR5 polymerase chain reaction
<input type="radio"/>	E. Antibodies to HIV-1

Next question

**HIV: seroconversion**

HIV seroconversion is symptomatic in 60-80% of patients and typically presents as a glandular fever type illness. Increased symptomatic severity is associated with poorer long term prognosis. It typically occurs 3-12 weeks after infection

**Features**

- sore throat
- lymphadenopathy
- malaise, myalgia, arthralgia
- diarrhoea
- maculopapular rash
- mouth ulcers
- rarely meningoencephalitis

**Diagnosis**

- antibodies to HIV may not be present
- HIV PCR and p24 antigen tests can confirm diagnosis

**Question 17 of 167**

Next

A 47-year-old lady is referred by her GP with a two day history of fever and headache. She is normally fit and well and has no past medical history of note. On examination you note nuchal rigidity. Investigations show the following:

Serum glucose	4.9 mmol/l
---------------	------------

Lumbar puncture reveals:

Opening pressure	14 cmCSF
Appearance	Cloudy
Glucose	1.7 mmol/l
Protein	1.9 g/l
White cells	900 / mm <sup>3</sup> (90% polymorphs)

What is the most likely infective agent?

<input type="radio"/>	A. <i>Streptococcus pneumoniae</i>
<input type="radio"/>	B. <i>E. coli</i>
<input type="radio"/>	C. <i>Listeria monocytogenes</i>
<input type="radio"/>	D. Enterovirus
<input type="radio"/>	E. <i>Streptococcus pyogenes</i>

Next question

The CSF results are consistent with bacterial meningitis (low glucose, high protein, high polymorphs). In this age group *Streptococcus pneumoniae* and *Neisseria meningitidis* are the most common causes of bacterial meningitis.

**Meningitis: causes**

0 - 3 months

- Group B *Streptococcus* (most common cause in neonates)
- *E. coli*
- *Listeria monocytogenes*

3 months - 6 years

- *Neisseria meningitidis*
- *Streptococcus pneumoniae*
- *Haemophilus influenzae*

6 years - 60 years

- *Neisseria meningitidis*
- *Streptococcus pneumoniae*

> 60 years

- *Streptococcus pneumoniae*
- *Neisseria meningitidis*
- *Listeria monocytogenes*

Immunosuppressed

- *Listeria monocytogenes*



A male child from a travelling community is diagnosed with measles. Which one of the following complications is he at risk from in the immediate aftermath of the initial infection?

<input type="radio"/>	A. Arthritis
<input type="radio"/>	B. Pancreatitis
<input type="radio"/>	C. Infertility
<input type="radio"/>	D. Subacute sclerosing panencephalitis
<input type="radio"/>	E. Pneumonia

Subacute sclerosing panencephalitis is seen but develops 5-10 years following the illness. Pancreatitis and infertility may follow mumps infection

## Measles

### Overview

- RNA paramyxovirus
- spread by droplets
- infective from prodrome until 5 days after rash starts
- incubation period = 10-14 days

### Features

- prodrome: irritable, conjunctivitis, fever
- Koplik spots (before rash): white spots ('grain of salt') on buccal mucosa
- rash: starts behind ears then to whole body, discrete maculopapular rash becoming blotchy & confluent

### Complications

- encephalitis: typically occurs 1-2 weeks following the onset of the illness)
- subacute sclerosing panencephalitis: very rare, may present 5-10 years following the illness
- febrile convulsions
- pneumonia, tracheitis
- keratoconjunctivitis, corneal ulceration
- diarrhoea
- increased incidence of appendicitis
- myocarditis

### Management of contacts

- if a child not immunized against measles comes into contact with measles then MMR should be offered (vaccine-induced measles antibody develops more rapidly than that following natural infection)
- this should be given within 72 hours

**Question 19 of 167**

Next

A 34-year-old postman attends the Emergency Department following a dog bite to his right hand. What is the most appropriate antibiotic therapy?

<input type="radio"/>	A. Metronidazole + amoxicillin
<input type="radio"/>	B. Erythromycin
<input type="radio"/>	C. Co-amoxiclav
<input type="radio"/>	D. Metronidazole
<input type="radio"/>	E. Flucloxacillin + penicillin

Next question

Animal bite - co-amoxiclav

A combination of doxycycline and metronidazole is recommended in the BNF if the patient is penicillin allergic

**Animal bites****Management**

- cleanse wound
- current BNF recommendation is co-amoxiclav
- if penicillin-allergic then doxycycline + metronidazole is recommended

You review a 14-year-old boy who has recently emigrated from Russia. He was involved in car accident two years ago and underwent an emergency splenectomy. Following this he takes penicillin V on a daily basis. He is unsure of his vaccination history. Which organism is he particularly susceptible to?

<input type="radio"/>	A. <i>Staphylococcus aureus</i>
<input type="radio"/>	B. HIV
<input type="radio"/>	C. <i>Haemophilus influenzae</i>
<input type="radio"/>	D. <i>Streptococcus pneumoniae</i>
<input type="radio"/>	E. <i>Mycobacterium tuberculosis</i>

[Next question](#)

Penicillin V would protect him against *Streptococcus pneumoniae* but not *Haemophilus influenzae* due to the production of beta-lactamases by the organism.

### Splenectomy

Following a splenectomy patients are particularly at risk from pneumococcus, Haemophilus, meningococcus and Capnocytophaga canimorsus\* infections

#### Vaccination

- if elective, should be done 2 weeks prior to operation
- Hib, meningitis A & C
- annual influenza vaccination
- pneumococcal vaccine every 5 years

#### Antibiotic prophylaxis

- penicillin V: unfortunately clear guidelines do not exist of how long antibiotic prophylaxis should be continued. It is generally accepted though that penicillin should be continued for at least 2 years and at least until the patient is 16 years of age, although the majority of patients are usually put on antibiotic prophylaxis for life

\*usually from dog bites

**Question 21 of 167**

Next

A 25-year-old man returns from a gap-year in Central and South America and presents with a 2 month history of an ulcerating lesion on his lower lip. Examination of his nasal and oral mucosae reveals widespread involvement. What is the likely cause?

<input type="radio"/>	A. <i>Leishmania brasiliensis</i>
<input type="radio"/>	B. <i>Leishmania mexicana</i>
<input type="radio"/>	C. <i>Trypanosoma cruzi</i>
<input type="radio"/>	D. Basal cell carcinoma
<input type="radio"/>	E. <i>Leishmania donovani</i>

Next question

Mucocutaneous ulceration following travel? - *Leishmania brasiliensis*

This patient most likely has leishmaniasis. The pattern of a primary skin lesion with mucosal involvement is characteristic of *Leishmania brasiliensis*

**Leishmaniasis**

Leishmaniasis is caused by the intracellular protozoa *Leishmania*, usually being spread by sand flies. Cutaneous, mucocutaneous leishmaniasis and visceral forms are seen

**Cutaneous leishmaniasis**

- caused by *Leishmania tropica* or *Leishmania mexicana*
- crusted lesion at site of bite
- may be underlying ulcer

**Mucocutaneous leishmaniasis**

- caused by *Leishmania brasiliensis*
- skin lesions may spread to involve mucosae of nose, pharynx etc

**Visceral leishmaniasis (kala-azar)**

- mostly caused by *Leishmania donovani*
- occurs Mediterranean, Asia, South America, Africa
- fever, sweats, rigors
- massive splenomegaly. hepatomegaly
- poor appetite\*, weight loss

- grey skin - 'kala-azar' means black sickness
- pancytopenia secondary to hypersplenism

\*occasionally patients may report increased appetite with paradoxical weight loss

**Question 22 of 167**

Next

A 33-year-old man who is HIV positive is admitted to the Emergency Department with confusion and drowsiness. A CT head shows multiple ring enhancing lesions. What is the most likely diagnosis?

<input type="radio"/>	A. Progressive multifocal leukoencephalopathy
<input type="radio"/>	B. Cryptococcal infection
<input type="radio"/>	C. Cerebral toxoplasmosis
<input type="radio"/>	D. CMV encephalitis
<input type="radio"/>	E. Tuberculosis

Next question

HIV - multiple ring enhancing lesions = toxoplasmosis

Cerebral toxoplasmosis is the most common neurological infection seen in HIV, occurring in up to 10% of patients

**HIV: neurocomplications****Generalised neurological disease****Encephalitis**

- may be due to CMV or HIV itself
- HSV encephalitis but is relatively rare in the context of HIV
- CT: oedematous brain

***Cryptococcus***

- most common fungal infection of CNS
- headache, fever, malaise, nausea/vomiting, seizures, focal neurological deficit
- CSF: high opening pressure, India ink test positive
- CT: meningeal enhancement, cerebral oedema
- meningitis is typical presentation but may occasionally cause a space occupying lesion

**Progressive multifocal leukoencephalopathy (PML)**

- widespread demyelination
- due to infection of oligodendrocytes by human papovirus (JC virus)
- symptoms, subacute onset : behavioural changes, speech, motor, visual impairment

- CT: single or multiple lesions, no mass effect, don't usually enhance. MRI is better - high-signal demyelinating white matter lesions are seen

#### AIDS dementia complex

- caused by HIV virus itself
- symptoms: behavioural changes, motor impairment
- CT: cortical and subcortical atrophy

### Focal neurological lesions

#### Toxoplasmosis

- accounts for around 50% of cerebral lesions in patients with HIV
- constitutional symptoms, headache, confusion, drowsiness
- CT: usually single or multiple ring enhancing lesions, mass effect may be seen
- management: sulfadiazine and pyrimethamine

#### Primary CNS lymphoma

- accounts for around 30% of cerebral lesions
- associated with the Epstein-Barr virus
- CT: single or multiple ring enhancing lesions

Differentiating between toxoplasmosis and lymphoma is a common clinical scenario in HIV patients. It is clearly important given the vastly different treatment strategies. The table below gives some general differences. Please see the Radiopaedia link for more details.

Toxoplasmosis	Lymphoma
Multiple lesions	Single lesion
Rng or nodular enhancement	Solid enhancement
Thallium SPECT negative	Thallium SPECT positive

#### Tuberculosis

- much less common than toxoplasmosis or primary CNS lymphoma
- CT: single enhancing lesion

A 30-year-old man is diagnosed as having malaria following a recent trip to Zimbabwe. Which one of the following is most likely to indicate severe malaria?

<input type="radio"/>	A. Parasitaemia 1%
<input type="radio"/>	B. Heart rate 102 per minute
<input type="radio"/>	C. White blood cells $18.2 \times 10^9/l$
<input type="radio"/>	D. Platelets $105 \times 10^9/l$
<input type="radio"/>	E. Respiratory rate 30 per minute

Next question

A respiratory rate of 30 per minute may indicate acute respiratory distress syndrome (ARDS), a feared complication of falciparum malaria. Whilst thrombocytopaenia can be caused by disseminated intravascular coagulation (DIC), it is also seen in many patients with uncomplicated malaria and hence would not automatically indicate severe malaria

### Malaria: Falciparum

Feature of severe malaria

- schizonts on a blood film
- parasitaemia > 2%
- hypoglycaemia
- temperature > 39 °C
- severe anaemia
- complications as below

Complications

- cerebral malaria: seizures, coma
- acute renal failure: blackwater fever, secondary to intravascular haemolysis, mechanism unknown
- acute respiratory distress syndrome (ARDS)
- hypoglycaemia
- disseminated intravascular coagulation (DIC)

Uncomplicated falciparum malaria

- strains resistant to chloroquine are prevalent in certain areas of Asia and Africa
- the 2010 WHO guidelines recommend artemisinin-based combination therapies (ACTs) as first-line therapy
- examples include artemether plus lumefantrine, artesunate plus amodiaquine, artesunate plus mefloquine, artesunate plus sulfadoxine-pyrimethamine, dihydroartemisinin plus piperaquine



## Severe falciparum malaria

- a parasite counts of more than 2% will usually need parenteral treatment irrespective of clinical state
- intravenous artesunate is now recommended by WHO in preference to intravenous quinine
- if parasite count > 10% then exchange transfusion should be considered
- shock may indicate coexistent bacterial septicaemia - malaria rarely causes haemodynamic collapse

A 30-year-old intravenous drug user is diagnosed as having osteomyelitis of the right tibia. What is the most likely causative organism?

<input type="radio"/>	A. <i>Salmonella</i> species
<input type="radio"/>	B. <i>Haemophilus influenzae</i>
<input type="radio"/>	C. <i>Staphylococcus aureus</i>
<input type="radio"/>	D. <i>Enterobacter</i> species
<input type="radio"/>	E. <i>Streptococcus pyogenes</i>

[Next question](#)

## Osteomyelitis

Osteomyelitis describes an infection of the bone.

*Staph. aureus* is the most common cause except in patients with sickle-cell anaemia where *Salmonella* species predominate.

Predisposing conditions

- diabetes mellitus
- sickle cell anaemia
- intravenous drug user
- immunosuppression due to either medication or HIV
- alcohol excess

Investigations

- MRI is the imaging modality of choice, with a sensitivity of 90-100%

Management

- flucloxacillin for 6 weeks
- clindamycin if penicillin-allergic

**Question 25 of 167**

Next

A 30-year-old woman presents with a white, malodorous vaginal discharge. There is no associated itch or dyspareunia. A diagnosis of bacterial vaginosis is suspected.

Overgrowth of which one of the following organisms is most likely to cause this presentation?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. <i>Lactobacilli</i>       |
| <input type="radio"/> | B. <i>Trichomonas</i>        |
| <input type="radio"/> | C. <i>Candida</i>            |
| <input type="radio"/> | D. <i>Mycoplasma hominis</i> |
| <input type="radio"/> | E. <i>Gardnerella</i>        |

Next question

Bacterial vaginosis - overgrowth of predominately *Gardnerella vaginalis*

**Bacterial vaginosis**

Bacterial vaginosis (BV) describes an overgrowth of predominately anaerobic organisms such as *Gardnerella vaginalis*. This leads to a consequent fall in lactic acid producing aerobic lactobacilli resulting in a raised vaginal pH.

Whilst BV is not a sexually transmitted infection it is seen almost exclusively in sexually active women.

**Features**

- vaginal discharge: 'fishy', offensive
- asymptomatic in 50%

Amsel's criteria for diagnosis of BV - 3 of the following 4 points should be present

- thin, white homogenous discharge
- clue cells on microscopy
- vaginal pH > 4.5
- positive whiff test (addition of potassium hydroxide results in fishy odour)

**Management**

- oral metronidazole for 5-7 days

- 70-80% initial cure rate
- relapse rate > 50% within 3 months
- the BNF suggests topical metronidazole or topical clindamycin as alternatives

#### Bacterial vaginosis in pregnancy

- results in an increased risk of preterm labour, low birth weight and chorioamnionitis, late miscarriage
- it was previously taught that oral metronidazole should be avoided in the first trimester and topical clindamycin used instead. Recent guidelines however recommend that oral metronidazole is used throughout pregnancy. The BNF still advises against the use of high dose metronidazole regimes

**Question 26 of 167**

Next

A 33-year-old woman who was diagnosed as having HIV-1 two years ago is reviewed in clinic. She is fit and well currently and has no symptoms of note. The only medication she takes is the occasional paracetamol for tension headaches. Her latest blood tests are as follows:

CD4	$325 \times 10^6/l$
-----	---------------------

What is the most appropriate action?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Wait until the CD4 count is below $200 \times 10^6/l$ |
| <input type="radio"/> | B. Wait until the CD4 count is above $350 \times 10^6/l$ |
| <input type="radio"/> | C. Wait until the CD4 count is below $250 \times 10^6/l$ |
| <input type="radio"/> | D. Start antiretroviral therapy now                      |
| <input type="radio"/> | E. Wait until the CD4 count is below $300 \times 10^6/l$ |

Next question

Start anti-retrovirals in HIV when  $CD4 < 350 \times 10^6/l$

**HIV: anti-retrovirals**

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

Protease inhibitors (PI)

- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system

A 19-year-old student is brought to the Emergency Department by friends due to a severe headache and drowsiness. On examination he has a widespread purpuric rash. Meningococcal infection is strongly suspected but he is known to be penicillin allergic (previous anaphylaxis). What is the antibiotic of choice?

<input type="radio"/>	A. Chloramphenicol
<input type="radio"/>	B. Meropenem
<input type="radio"/>	C. Teicoplanin
<input type="radio"/>	D. Erythromycin
<input type="radio"/>	E. Ciprofloxacin

Next question

### Meningitis: management

Investigations suggested by NICE

- full blood count
- CRP
- coagulation screen
- blood culture
- whole-blood PCR
- blood glucose
- blood gas

Lumbar puncture if no signs of raised intracranial pressure

### Management

All patients should be transferred to hospital urgently. If patients are in a pre-hospital setting (for example a GP surgery) and meningococcal disease is suspected then intramuscular benzylpenicillin may be given, as long as this doesn't delay transit to hospital.

BNF recommendations on antibiotics

Initial empirical therapy aged 3 months - 50 years	Intravenous cefotaxime
Initial empirical therapy aged > 50 years	Intravenous cefotaxime + amoxicillin
Meningococcal meningitis	Intravenous benzylpenicillin or cefotaxime
Pneumococcal meningitis	Intravenous cefotaxime
Meningitis caused by <i>Haemophilus influenzae</i>	Intravenous cefotaxime
Meningitis caused by <i>Listeria</i>	Intravenous amoxicillin + gentamicin

If the patient has a history of immediate hypersensitivity reaction to penicillin or to cephalosporins the BNF recommends using chloramphenicol.

#### Management of contacts

- prophylaxis needs to be offered to household and close contacts of patients affected with meningococcal meningitis
- oral rifampicin or ciprofloxacin may be used
- the risk is highest in the first 7 days but persists for at least 4 weeks
- meningococcal vaccination should be offered when serotype results are available, for close contacts who have not previously been vaccinated



**Question 28 of 167**

Next

A 43-year-old man from South Africa is reviewed in clinic. He has recently started treatment for tuberculosis but is complaining of a deterioration in his vision. Which one of the following drugs is most likely to cause decreased visual acuity?

<input type="radio"/>	A. Rifampicin
<input type="radio"/>	B. Streptomycin
<input type="radio"/>	C. Isoniazid
<input checked="" type="radio"/>	D. Ethambutol
<input type="radio"/>	E. Pyrazinamide

Next question

Optic neuritis is common in patients taking ethambutol

Isoniazid may also cause optic neuritis but it is not as common a cause as ethambutol.

**Tuberculosis: drug side-effects**

Common side effects:

Rifampicin

- potent liver enzyme inducer
- hepatitis, orange secretions
- flu-like symptoms

Isoniazid

- peripheral neuropathy: prevent with pyridoxine (Vitamin B6)
- hepatitis, agranulocytosis
- liver enzyme inhibitor

Pyrazinamide

- hyperuricaemia causing gout
- hepatitis

Ethambutol

- optic neuritis: check visual acuity before and during treatment
- dose needs adjusting in patients with renal impairment

Which one of the following statements is true regarding *Listeria monocytogenes*?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Multiplies rapidly at high temperatures            |
| <input type="radio"/> | B. The organism is resistant to ampicillin            |
| <input type="radio"/> | C. It is a Gram negative bacillus                     |
| <input type="radio"/> | D. It is diagnosed by the presence of urinary antigen |
| <input type="radio"/> | E. May cause ataxia                                   |

Next question

## Listeria

*Listeria monocytogenes* is a Gram positive bacillus which has the unusual ability to multiply at low temperatures. It is typically spread via contaminated food, typically unpasteurised dairy products. Infection is particularly dangerous to the unborn child where it can lead to miscarriage

Features - can present in a variety of ways

- diarrhoea, flu-like illness
- pneumonia , meningoencephalitis
- ataxia and seizures

Suspected *Listeria* infection should be investigated by taking blood cultures. CSF may reveal a pleocytosis, with 'tumbling motility' on wet mounts

Management

- *Listeria* is sensitive to amoxicillin/ampicillin (cephalosporins usually inadequate)
- *Listeria* meningitis should be treated with IV amoxicillin/ampicillin and gentamicin

Following a diagnosis of tetanus, what is the most appropriate antibiotic therapy to give with human tetanus immunoglobulin?

<input type="radio"/>	A. IV clarithromycin
<input type="radio"/>	B. IV benzylpenicillin
<input type="radio"/>	C. IV gentamicin
<input type="radio"/>	D. IV metronidazole
<input type="radio"/>	E. IV ciprofloxacin

[Next question](#)

## Tetanus

Tetanus is caused by the tetanospasmin exotoxin released from *Clostridium tetani*. Tetanus spores are present in soil and may be introduced into the body from a wound, which is often unnoticed. Tetanospasmin prevents release of GABA

### Features

- prodrome fever, lethargy, headache
- trismus (lockjaw)
- risus sardonicus
- opisthotonus (arched back, hyperextended neck)
- spasms (e.g. dysphagia)

### Management

- supportive therapy including ventilatory support and muscle relaxants
- intramuscular human tetanus immunoglobulin for high-risk wounds (e.g. compound fractures, delayed surgical intervention, significant degree of devitalised tissue)
- metronidazole is now preferred to benzylpenicillin as the antibiotic of choice

Which one of the following congenital infections is most characteristically associated with sensorineural deafness?

- ☐ A. *Toxoplasma gondii*
- ☐ B. Parvovirus B19
- ☐ C. Rubella
- ☐ D. *Treponema pallidum*
- ☐ E. Cytomegalovirus

Next question

#### Congenital rubella

- sensorineural deafness
- congenital cataracts

### Congenital infections

The major congenital infections encountered in examinations are rubella, toxoplasmosis and cytomegalovirus

Cytomegalovirus is the most common congenital infection in the UK. Maternal infection is usually asymptomatic

	Rubella	Toxoplasmosis	Cytomegalovirus
<b>Characteristic features</b>	Sensorineural deafness Congenital cataracts Congenital heart disease (e.g. patent ductus arteriosus) Glaucoma	Cerebral calcification Chorioretinitis Hydrocephalus	Growth retardation Purpuric skin lesions
<b>Other features</b>	Growth retardation Hepatosplenomegaly Purpuric skin lesions 'Salt and pepper' chorioretinitis Microphthalmia Cerebral palsy	Anaemia Hepatosplenomegaly Cerebral palsy	Sensorineural deafness Encephalitis Pneumonitis Hepatosplenomegaly Anaemia Jaundice Cerebral palsy

A 31-year-old man who is known to be HIV positive presents with dyspnoea and a dry cough. He is currently homeless and has not been attending his outpatient appointments or taking antiretroviral medication. Clinical examination reveals a respiratory rate of 24 / min. Chest auscultation is unremarkable with only scattered crackles. His oxygen saturation is 96% on room air but this falls rapidly after walking the length of the ward. Given the likely diagnosis, what is the most appropriate first-line treatment?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Fluconazole                    |
| <input type="radio"/> | B. Co-trimoxazole                 |
| <input type="radio"/> | C. Erythromycin                   |
| <input type="radio"/> | D. Ganciclovir                    |
| <input type="radio"/> | E. Sulfadiazine and pyrimethamine |

[Next question](#)

### HIV: *Pneumocystis jiroveci* pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as *Pneumocystis jiroveci*, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- *Pneumocystis jiroveci* is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count  $< 200/\text{mm}^3$  should receive PCP prophylaxis

#### Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Extrapulmonary manifestations are rare (1-2% of cases), may cause

- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

#### Investigation

- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal
- exercise-induced desaturation
- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain)

## Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if  $pO_2 < 9.3\text{kPa}$  then steroids reduce risk of respiratory failure by 50% and death by a third)

A 19-year-old man presents with a compound fracture of his leg following a fall from scaffolding. Examination reveals soiling of the wound with mud. He is sure he has had five previous tetanus vaccinations. What is the most appropriate course of action to prevent the development of tetanus?

<input type="radio"/>	A. Clean wound + intramuscular human tetanus immunoglobulin
<input type="radio"/>	B. Clean wound + tetanus vaccine
<input type="radio"/>	C. Clean wound + tetanus vaccine + intramuscular human tetanus immunoglobulin
<input type="radio"/>	D. Clean wound + tetanus vaccine + benzylpenicillin
<input type="radio"/>	E. Clean wound

[Next question](#)

A soiled, compound fracture is regarded as high-risk for tetanus and intramuscular human tetanus immunoglobulin should be given. There is a role for antibiotics given the soiled wound although benzylpenicillin would not be the drug of choice.

### Tetanus: vaccination

The tetanus vaccine is a cell-free purified toxin that is normally given as part of a combined vaccine.

Tetanus vaccine is currently given in the UK as part of the routine immunisation schedule at:

- 2 months
- 3 months
- 4 months
- 3-5 years
- 13-18 years

This therefore provides 5 doses of tetanus-containing vaccine. Five doses is now considered to provide adequate long-term protection against tetanus.

Intramuscular human tetanus immunoglobulin should be given to patients with high-risk wounds (e.g. Compound fractures, delayed surgical intervention, significant degree of devitalised tissue) irrespective of whether 5 doses of tetanus vaccine have previously been given

If vaccination history is incomplete or unknown then a dose of tetanus vaccine should be given combined with intramuscular human tetanus immunoglobulin for high-risk wounds

A 44-year-old farmer presents with headache, fever and muscle aches. He initially thought he had a bad cold but his symptoms have got progressively worse over the past week. During the review of systems he reports nausea and a decreased urine output. On examination his temperature is 38.2°C, pulse 102 / min and his chest is clear. Subconjunctival haemorrhages are noted but there is no evidence of jaundice. What is the most likely diagnosis?

<input type="radio"/>	A. Mycoplasma pneumonia
<input type="radio"/>	B. Lyme disease
<input type="radio"/>	C. Legionella pneumonia
<input type="radio"/>	D. Listeria
<input type="radio"/>	E. Leptospirosis

[Next question](#)

The main clue in the question is the patients occupation. Mycoplasma and Legionella are less likely due to the absence of chest symptoms and signs. Liver failure is seen in only 10% of patients with leptospirosis..

### Leptospirosis

Also known as Weil's disease\*, leptospirosis is commonly seen in questions referring to sewage workers, farmers, vets or people who work in abattoir. It is caused by the spirochaete *Leptospira interrogans* (serogroup L icterohaemorrhagiae), classically being spread by contact with infected rat urine. Weil's disease should always be considered in high-risk patients with hepatorenal failure

#### Features

- fever
- flu-like symptoms
- renal failure (seen in 50% of patients)
- jaundice
- subconjunctival haemorrhage
- headache, may herald the onset of meningitis

#### Management

- high-dose benzylpenicillin or doxycycline

\*the term Weil's disease is sometimes reserved for the most severe 10% of cases that are associated with jaundice



A 57-year-old female presents with headache and fever to the Emergency Department. On examination neck stiffness is noted along with a positive Kernig's sign. A lumbar puncture is performed and reported as follows:

CSF culture	Gram positive bacilli
-------------	-----------------------

What is the most likely causative organism?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. <i>Cryptococcus</i>             |
| <input type="radio"/> | B. <i>Haemophilus influenzae</i>   |
| <input type="radio"/> | C. <i>Streptococcus pneumoniae</i> |
| <input type="radio"/> | D. <i>E. coli</i>                  |
| <input type="radio"/> | E. <i>Listeria monocytogenes</i>   |

Next question

### Classification of bacteria

Remember:

- Gram positive cocci = staphylococci + streptococci (including enterococci)
- Gram negative cocci = *Neisseria meningitidis* + *Neisseria gonorrhoeae*, also *Moraxella*

Therefore, only a small list of Gram positive rods (bacilli) need to be memorised to categorise all bacteria - mnemonic = ABCD L

- *Actinomyces*
- *Bacillus anthracis* (anthrax)
- *Clostridium*
- Diphtheria: *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

Remaining organisms are Gram negative rods

Which one of the following is true regarding linezolid?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Active against both MRSA and VRE (Vancomycin-Resistant Enterococcus)               |
| <input type="radio"/> | B. Bactericidal in action   |
| <input type="radio"/> | C. No activity against GISA (Glycopeptide Intermediate <i>Staphylococcus aureus</i> ) |
| <input type="radio"/> | D. Adverse effects include raised platelet count                                      |
| <input type="radio"/> | E. Inhibits RNA synthesis   |

Next question

### Linezolid

Linezolid is a type of oxazolidinone antibiotic which has been introduced in recent years. It inhibits bacterial protein synthesis by stopping formation of the 70s initiation complex and is bacteriostatic nature

Spectrum, highly active against Gram positive organisms including:

- MRSA (Methicillin-resistant *Staphylococcus aureus*)
- VRE (Vancomycin-resistant enterococcus)
- GISA (Glycopeptide Intermediate *Staphylococcus aureus*)

Adverse effects

- thrombocytopenia (reversible on stopping)
- monoamine oxidase inhibitor: avoid tyramine containing foods

**Question 37 of 167**

Next

A 43-year-old Asian man presents with headache and neck stiffness. CT brain is normal and a lumbar puncture is performed with the following results

Serum glucose	4.7 mmol/l
---------------	------------

Lumbar puncture reveals:

Opening pressure	15 cmCSF
Appearance	Cloudy
Glucose	3.3 mmol/l
Protein	0.7 g/l
White cells	100 / mm <sup>3</sup> (70% lymphocytes)

What is the most likely diagnosis?

<input type="radio"/>	A. Bacterial meningitis
<input type="radio"/>	B. Viral meningitis
<input type="radio"/>	C. Tuberculous meningitis
<input type="radio"/>	D. Normal CSF result
<input type="radio"/>	E. Cryptococcal meningitis

Next question

The CSF lymphocytosis combined with a glucose greater than half the serum level points towards a viral meningitis. TB meningitis is associated with a low CSF glucose

**Meningitis: CSF analysis**

The table below summarises the characteristic cerebrospinal fluid (CSF) findings in meningitis:

	<b>Bacterial</b>	<b>Viral</b>	<b>Tuberculous</b>
<b>Appearance</b>	Cloudy	Clear/cloudy	Fibrin web
<b>Glucose</b>	Low (< 1/2 plasma)	Normal*	Low (< 1/2 plasma)
<b>Protein</b>	High (> 1 g/l)	Normal/raised	High (> 1 g/l)
<b>White cells</b>	10 - 5,000 polymorphs/mm <sup>3</sup>	15 - 1,000 lymphocytes/mm <sup>3</sup>	10 - 1,000 lymphocytes/mm <sup>3</sup>

The Ziehl-Neelsen stain is only 20% sensitive in the detection of tuberculous meningitis and therefore PCR is sometimes used (sensitivity = 75%)

\*mumps is unusual in being associated with a low glucose level in a proportion of cases. A low glucose may also be seen in herpes encephalitis

Serum glucose	4.9 mmol/l
---------------	------------

**Lumbar puncture reveals:**

Opening pressure	14 cmCSF
Appearance	Cloudy
Glucose	1.7 mmol/l
Protein	1.9 g/l
White cells	900 / mm <sup>3</sup> (90% polymorphs)

A 23-year-old woman comes for review. She has had recurrent genital warts for the past 4 years which have failed to respond to topical podophyllum. On one occasion she had cryotherapy but will not have it again due to local discomfort. On examination she has a large number of fleshy genital warts around her introitus. What is the most appropriate next step in treatment?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Topical glutaraldehyde |
| <input type="radio"/> | B. Oral podophyllum       |
| <input type="radio"/> | C. Topical imiquimod      |
| <input type="radio"/> | D. Oral aciclovir         |
| <input type="radio"/> | E. Topical salicylic acid |

[Next question](#)

## Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16, 18 & 33) predisposes to cervical cancer.

### Features

- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

### Management

- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment and recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

A 30-year-old man presents to the genito-urinary medicine clinic. He has been handed a slip from an ex-girlfriend stating she has tested positive for *Chlamydia*. He last slept with her 2 months ago. He has no symptoms of note, in particular no dysuria or discharge. What is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Reassure symptoms would have presented by now   |
| <input type="radio"/> | B. Offer antibiotic therapy  |
| <input type="radio"/> | C. Offer <i>Chlamydia</i> testing and antibiotic treatment immediately without waiting for the results |
| <input type="radio"/> | D. Offer <i>Chlamydia</i> testing and antibiotic treatment if positive                                 |
| <input type="radio"/> | E. Notify public health  |

[Next question](#)

Treatment is given on the basis of exposure to infection rather than proven infection

### ***Chlamydia***

*Chlamydia* is the most prevalent sexually transmitted infection in the UK and is caused by *Chlamydia trachomatis*, an obligate intracellular pathogen. Approximately 1 in 10 young women in the UK have *Chlamydia*. The incubation period is around 7-21 days, although it should be remembered a large percentage of cases are asymptomatic

#### Features

- asymptomatic in around 70% of women and 50% of men
- women: cervicitis (discharge, bleeding), dysuria
- men: urethral discharge, dysuria

#### Potential complications

- epididymitis
- pelvic inflammatory disease
- endometritis
- increased incidence of ectopic pregnancies
- infertility
- reactive arthritis
- perihepatitis (Fitz-Hugh-Curtis syndrome)

#### Investigation

- traditional cell culture is no longer widely used
- nuclear acid amplification tests (NAATs) are now rapidly emerging as the investigation of choice

- urine (first void urine sample), vulvovaginal swab or cervical swab may be tested using the NAAT technique

## Screening

- in England the National *Chlamydia* Screening Programme is open to all men and women aged 15-24 years
- the 2009 SIGN guidelines support this approach, suggesting screening all sexually active patients aged 15-24 years
- relies heavily on opportunistic testing

## Management

- doxycycline (7 day course) or azithromycin (single dose). The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline
- if pregnant then erythromycin or amoxicillin may be used. The SIGN guidelines suggest considering azithromycin 'following discussion of the balance of benefits and risks with the patient'
- patients diagnosed with *Chlamydia* should be offered a choice of provider for initial partner notification - either trained practice nurses with support from GUM, or referral to GUM
- for men with symptomatic infection all partners from the four weeks prior to the onset of symptoms should be contacted
- for women and asymptomatic men all partners from the last six months or the most recent sexual partner should be contacted
- contacts of confirmed *Chlamydia* cases should be offered treatment prior to the results of their investigations being known (treat then test)

A 33-year-old man is admitted due to profuse diarrhoea. He has a history of HIV infection and *Cryptosporidium* diarrhoea is suspected. What investigation is most likely to confirm the diagnosis?

<input type="radio"/>	A. Blood cultures
<input type="radio"/>	B. Sigmoidoscopy with biopsy
<input type="radio"/>	C. Abdominal x-ray
<input type="radio"/>	D. Acid-fast staining of stool sample
<input type="radio"/>	E. <i>Cryptosporidium</i> PCR of stool sample

[Next question](#)

*Cryptosporidium* cysts turn red following acid-fast staining. Molecular methods are currently used mainly as a research tool

#### HIV: diarrhoea

Diarrhoea is common in patients with HIV. This may be due to the effects of the virus itself (HIV enteritis) or opportunistic infections

Possible causes

- *Cryptosporidium* + other protozoa (most common)
- Cytomegalovirus
- *Mycobacterium avium intracellulare*
- *Giardia*

*Cryptosporidium* is the most common infective cause of diarrhoea in HIV patients. It is an intracellular protozoa and has an incubation period of 7 days. Presentation is very variable, ranging from mild to severe diarrhoea. A modified Ziehl-Neelsen stain (acid-fast stain) of the stool may reveal the characteristic red cysts of *Cryptosporidium*. Treatment is difficult, with the mainstay of management being supportive therapy\*

*Mycobacterium avium intracellulare* is an atypical mycobacteria seen with the CD4 count is below 50. Typical features include fever, sweats, abdominal pain and diarrhoea. There may be hepatomegaly and deranged LFTs. Diagnosis is made by blood cultures and bone marrow examination. Management is with rifabutin, ethambutol and clarithromycin

\*nitazoxanide is licensed in the US for immunocompetent patients



A 62-year-old patient with type 2 diabetes mellitus presents with a 'rash' on his left shin. This has grown in size over the past two days and is now a painful, hot, erythematous area on his anterior left shin spreading around to the back of the leg. He is systemically well and a decision is made to give oral treatment. He has a past history of penicillin allergy. What is the most appropriate antibiotic to give?

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. Ciprofloxacin  |
| <input type="radio"/> | B. Cefaclor       |
| <input type="radio"/> | C. Flucloxacillin |
| <input type="radio"/> | D. Vancomycin     |
| <input type="radio"/> | E. Clarithromycin |

[Next question](#)

### Cellulitis: management

The BNF recommends flucloxacillin as first-line treatment for mild/moderate cellulitis. Clarithromycin or clindamycin is recommended in patients allergic to penicillin.

Many local protocols now suggest the use of oral clindamycin in patients who have failed to respond to flucloxacillin.

Severe cellulitis should be treated with intravenous benzylpenicillin + flucloxacillin.

A 72-year-old woman is reviewed following a course of oral flucloxacillin for right lower limb cellulitis. The local protocol suggest oral clindamycin should be used next-line. Which one of the following side-effects is it most important to warn her about?

<input type="radio"/>	A. Heartburn or indigestion
<input type="radio"/>	B. Jaundice
<input type="radio"/>	C. Sore throat, bruising or lethargy
<input type="radio"/>	D. Avoid any food or drink containing alcohol
<input type="radio"/>	E. Diarrhoea

[Next question](#)

### ***Clostridium difficile***

*Clostridium difficile* is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading cause of *Clostridium difficile*.

#### Features

- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

#### Management

- first-line therapy is oral metronidazole for 10-14 days
- if severe or not responding to metronidazole then oral vancomycin may be used
- for life-threatening infections a combination of oral vancomycin and intravenous metronidazole should be used

A 37-year-old immigrant from Bolivia is admitted to the Emergency Department following a collapse. He is known to have a history of Chagas' disease. Which one of the following complications of Chagas' disease accounts for the majority of mortality in affected patients?

<input type="radio"/>	A. Large bowel perforation secondary to megacolon
<input type="radio"/>	B. Myocarditis
<input type="radio"/>	C. Perinephric abscess
<input type="radio"/>	D. Meningoencephalitis
<input type="radio"/>	E. Pulmonary haemorrhage

Cardiac involvement is the leading cause of death in patients with Chagas' disease

### Trypanosomiasis

Two main form of this protozoal disease are recognised - African trypanosomiasis (sleeping sickness) and American trypanosomiasis (Chagas' disease)

Two forms of **African trypanosomiasis**, or **sleeping sickness**, are seen - *Trypanosoma gambiense* in West Africa and *Trypanosoma rhodesiense* in East Africa. Both types are spread by the tsetse fly. *Trypanosoma rhodesiense* tends to follow a more acute course. Clinical features include:

- Trypanosoma chancre - tender subcutaneous nodule at site of infection
- enlargement of posterior cervical lymph nodes
- later: central nervous system involvement e.g. meningoencephalitis

#### Management

- early disease: IV pentamidine or suramin
- later disease or central nervous system involvement: IV melarsoprol

**American trypanosomiasis**, or **Chagas' disease**, is caused by the protozoan *Trypanosoma cruzi*. The vast majority of patients (95%) are asymptomatic in the acute phase although a chagoma (an erythematous nodule at site of infection) and periorbital oedema are sometimes seen. Chronic Chagas' disease mainly affects the heart and gastrointestinal tract

- myocarditis may lead to heart failure and arrhythmias
- gastrointestinal features includes megaesophagus and megacolon causing dysphagia and constipation

#### Management

- treatment is most effective in the acute phase using azole or nitroderivatives such as benznidazole or nifurtimox
- chronic disease management involves treating the complications e.g., heart failure

A 31-year-old woman presents as she has noted an offensive, fishy vaginal discharge. She describes a grey, watery discharge. What is the most likely diagnosis?

<input type="radio"/>	A. <i>Trichomonas vaginalis</i>
<input type="radio"/>	B. <i>Candida</i>
<input type="radio"/>	C. <i>Chlamydia</i>
<input type="radio"/>	D. Bacterial vaginosis
<input type="radio"/>	E. Physiological discharge

Next question

## Vaginal discharge

Vaginal discharge is a common presenting symptom and is not always pathological

Common causes

- physiological
- *Candida*
- *Trichomonas vaginalis*
- bacterial vaginosis

Less common causes

- whilst cervical infections such as *Chlamydia* and Gonorrhoea can cause a vaginal discharge this is rarely the presenting symptoms
- ectropion
- foreign body
- cervical cancer

Key features of the common causes are listed below

Condition	Key features
<i>Candida</i>	'Cottage cheese' discharge Vulvitis Itch
<i>Trichomonas vaginalis</i>	Offensive, yellow/green, frothy discharge Vulvovaginitis Strawberry cervix
Bacterial vaginosis	Offensive, thin, white/grey, 'fishy' discharge

Which one of the following statements regarding scabies is false?

<input type="radio"/>	A. All members of the household should be treated
<input type="radio"/>	B. Typically affects the fingers, interdigital webs and flexor aspects of the wrist in adults
<input type="radio"/>	C. Scabies causes a delayed type IV hypersensitivity reaction
<input type="radio"/>	D. Patients who complain of pruritus 4 weeks following treatment should be retreated
<input type="radio"/>	E. Malathion is suitable for the eradication of scabies

Next question

It is normal for pruritus to persist for up to 4-6 weeks post eradication

### Scabies

Scabies is caused by the mite *Sarcoptes scabiei* and is spread by prolonged skin contact. It typically affects children and young adults.

The scabies mite burrows into the skin, laying its eggs in the stratum corneum. The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

#### Features

- widespread pruritus
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

#### Management

- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication

#### Patient guidance on treatment (from Clinical Knowledge Summaries)

- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic
- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation. Patients should be given the following instructions:

- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8-12 hours for permethrin, or for 24 hours for malathion, before washing off
- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

A 44-year-old farmer presents to the Emergency Department due to a high temperature and confusion. On examination his pulse is 124 bpm, blood pressure 84/56 mmHg and temperature 39.8°C. He has a generalised erythematous rash which is starting to desquamate on his palms and is also noted to have a paronychia infection of a fingernail on the left hand. What is the most likely diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Paraquat overdose                     |
| <input type="radio"/> | B. Leptospirosis                         |
| <input type="radio"/> | C. Staphylococcal toxic shock syndrome   |
| <input type="radio"/> | D. Disseminated herpes simplex infection |
| <input type="radio"/> | E. Organophosphate poisoning             |

[Next question](#)

### Staphylococcal toxic shock syndrome

Staphylococcal toxic shock syndrome describes a severe systemic reaction to staphylococcal exotoxins. It came to prominence in the early 1980's following a series of cases related to infected tampons

Centers for Disease Control and Prevention diagnostic criteria

- fever: temperature  $> 38.9^{\circ}\text{C}$
- hypotension: systolic blood pressure  $< 90$  mmHg
- diffuse erythematous rash
- desquamation of rash, especially of the palms and soles
- involvement of three or more organ systems: e.g. gastrointestinal (diarrhoea and vomiting), mucous membrane erythema, renal failure, hepatitis, thrombocytopenia, CNS involvement (e.g. confusion)

A 45-year-old man presents to the Emergency Department due to severe pain in the perineal area over the past 6 hours. On examination the skin is cellulitic, extremely tender and haemorrhagic bullae are seen. What is the most appropriate management?

<input type="radio"/>	A. Surgical debridement
<input type="radio"/>	B. IV cefuroxime and metronidazole
<input type="radio"/>	C. IV flucloxacillin and benzylpenicillin
<input type="radio"/>	D. Plasma exchange
<input type="radio"/>	E. Urgent microscopy of wound swab

[Next question](#)

Surgical referral is the single most important step in the management of necrotising fasciitis. There has been little change in the mortality of necrotising fasciitis since the introduction of antibiotics

### Necrotising fasciitis

Necrotising fasciitis is a medical emergency that is difficult to recognise in the early stages

It can be classified according to the causative organism:

- type 1 is caused by mixed anaerobes and aerobes (often occurs post-surgery in diabetics)
- type 2 is caused by *Streptococcus pyogenes*

### Features

- acute onset
- painful, erythematous lesion develops
- extremely tender over infected tissue

### Management

- urgent surgical referral debridement
- intravenous antibiotics



Which one of the following features is least likely to occur in a patient with visceral leishmaniasis?

<input type="radio"/>	A. Massive splenomegaly
<input type="radio"/>	B. Diarrhoea
<input type="radio"/>	C. Pyrexia
<input type="radio"/>	D. Pancytopenia
<input type="radio"/>	E. Grey skin

Next question

The most common symptoms seen in patients with visceral leishmaniasis are pyrexia, splenomegaly (which is often massive), weight loss and night sweats. Pancytopenia occurs secondary to hypersplenism. Diarrhoea is not a typical feature

### Leishmaniasis

Leishmaniasis is caused by the intracellular protozoa *Leishmania*, usually being spread by sand flies. Cutaneous, mucocutaneous leishmaniasis and visceral forms are seen

#### Cutaneous leishmaniasis

- caused by *Leishmania tropica* or *Leishmania mexicana*
- crusted lesion at site of bite
- may be underlying ulcer

#### Mucocutaneous leishmaniasis

- caused by *Leishmania brasiliensis*
- skin lesions may spread to involve mucosae of nose, pharynx etc

#### Visceral leishmaniasis (kala-azar)

- mostly caused by *Leishmania donovani*
- occurs Mediterranean, Asia, South America, Africa
- fever, sweats, rigors
- massive splenomegaly. hepatomegaly
- poor appetite\*, weight loss
- grey skin - 'kala-azar' means black sickness
- pancytopenia secondary to hypersplenism

\*occasionally patients may report increased appetite with paradoxical weight loss

You attend a meeting with the hospital management. There is currently an increased incidence of MRSA septicaemia in the hospital and a strategy is being drawn up to tackle this. What is the most effective single step to reduce the incidence of MRSA?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. The use of personal protective equipment for staff including gloves and aprons |
| <input type="radio"/> | B. Hand hygiene   |
| <input type="radio"/> | C. Screening patients for MRSA on admission                                       |
| <input type="radio"/> | D. Cohort nursing   |
| <input type="radio"/> | E. Limiting the number of visitors  |

[Next question](#)

Whilst tackling MRSA requires a multi-pronged approach the evidence base demonstrates that hand hygiene is the single most important step

## MRSA

Methicillin-resistant *Staphylococcus aureus* (MRSA) was one of the first organisms which highlighted the dangers of hospital-acquired infections.

Who should be screened for MRSA?

- all patients awaiting elective admissions (exceptions include day patients having terminations of pregnancy and ophthalmic surgery. Patients admitted to mental health trusts are also excluded)
- from 2011 all emergency admissions will be screened

How should a patient be screened for MRSA?

- nasal swab and skin lesions or wounds
- the swab should be wiped around the inside rim of a patient's nose for 5 seconds
- the microbiology form must be labelled 'MRSA screen'

Suppression of MRSA from a carrier once identified

- nose: mupirocin 2% in white soft paraffin, tds for 5 days
- skin: chlorhexidine gluconate, od for 5 days. Apply all over but particularly to the axilla, groin and perineum

The following antibiotics are commonly used in the treatment of MRSA infections:

- vancomycin

- teicoplanin

Some strains may be sensitive to the antibiotics listed below but they should not generally be used alone because resistance may develop:

- rifampicin
- macrolides
- tetracyclines
- aminoglycosides
- clindamycin

Relatively new antibiotics such as linezolid, quinupristin/dalfopristin combinations and tigecycline have activity against MRSA but should be reserved for resistant cases

A newly qualified staff nurse at the local hospital undergoes vaccination against hepatitis B. The following results are obtained three months after completion of the primary course:

Anti-HBs	10 - 100 mIU/ml
----------	-----------------

What is the most appropriate course of action?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Repeat course (i.e. 3 doses) of hepatitis B vaccine   |
| <input type="radio"/> | B. Repeat anti-HBs level in three months time  |
| <input type="radio"/> | C. Give a course of hepatitis B immune globulin (HBIG) + one further dose of hepatitis B vaccine |
| <input type="radio"/> | D. Give one further dose of hepatitis B vaccine  |
| <input type="radio"/> | E. Do a HIV test   |

Next question

## Hepatitis B

Hepatitis B is a double-stranded DNA virus and is spread through exposure to infected blood or body fluids, including vertical transmission from mother to child. The incubation period is 6-20 weeks.

Immunisation against hepatitis B (please see the Greenbook link for more details)

- contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology
- most schedules give 3 doses of the vaccine with a recommendation for a one-off booster 5 years following the initial primary vaccination
- at risk groups who should be vaccinated include: healthcare workers, intravenous drug users, sex workers, close family contacts of an individual with hepatitis B, individuals receiving blood transfusions regularly, chronic kidney disease patients who may soon require renal replacement therapy, prisoners, chronic liver disease patients
- around 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine. Risk factors include age over 40 years, obesity, smoking, alcohol excess and immunosuppression
- testing for anti-HBs is only recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease. In these patients anti-HBs levels should be checked 1-4 months after primary immunisation
- the table below shows how to interpret anti-HBs levels:

Anti-HBs level (mIU/ml)	Response
-------------------------	----------

> 100	Indicates adequate response, no further testing required. Should still receive booster at 5 years
10 - 100	Suboptimal response - one additional vaccine dose should be given. If immunocompetent no further testing is required
< 10	Non-responder. Test for current or past infection. Give further vaccine course (i.e. 3 doses again) with testing following. If still fails to respond then HBIG would be required for protection if exposed to the virus

### Complications of hepatitis B infection

- chronic hepatitis (5-10%)
- fulminant liver failure (1%)
- hepatocellular carcinoma
- glomerulonephritis
- polyarteritis nodosa
- cryoglobulinaemia

### Management of hepatitis B

- pegylated interferon-alpha used to be the only treatment available. It reduces viral replication in up to 30% of chronic carriers. A better response is predicted by being female, < 50 years old, low HBV DNA levels, non-Asian, HIV negative, high degree of inflammation on liver biopsy
- however due to the side-effects of pegylated interferon it is now used less commonly in clinical practice. Oral antiviral medication is increasingly used with an aim to suppress viral replication (not in dissimilar way to treating HIV patients)
- examples include lamivudine, tenofovir and entecavir

You are reviewing test results. The midstream specimen of urine (MSU) from a 24-year-old woman who is 11 weeks pregnant shows a urinary tract infection. On discussing the result with the patient she does describe some dysuria and 'smelly urine'. What is the most appropriate management?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Ciprofloxacin for 7 days |
| <input type="radio"/> | B. Amoxicillin for 7 days   |
| <input type="radio"/> | C. Repeat MSU               |
| <input type="radio"/> | D. Trimethoprim for 3 days  |
| <input type="radio"/> | E. No treatment             |

[Next question](#)

As this woman is symptomatic she should be treated with an antibiotic that is safe to use in pregnancy.

### Urinary tract infection in adults: management

Lower urinary tract infections in women (cystitis)

- local antibiotic guidelines should be followed if available
- Clinical Knowledge Summaries (CKS) recommend trimethoprim or nitrofurantoin for 3 days

Lower urinary tract infections in pregnancy

- asymptomatic bacteriuria is screened for on the booking visit. If found, it should be confirmed with a second MSU and treated if confirmed (please see CKS link for more details)
- for acute lower urinary tract infections consider amoxicillin or an oral cephalosporin for 7 days\*

For patients with sign of acute pyelonephritis hospital admission should be considered

- local antibiotic guidelines should be followed if available
- the BNF currently recommends a broad-spectrum cephalosporin or a quinolone for 10-14 days
- Clinical Knowledge Summaries recommend ciprofloxacin for 7 days or co-amoxiclav for 14 days

\*CKS also mention the use of trimethoprim and nitrofurantoin. Trimethoprim is a folate antagonist and concerns have been raised regarding the potential risk of neural tube defects. Manufacturers advise to avoid. Whilst short-term trimethoprim use is unlikely to cause folate deficiency it would seem reasonable to use an antibiotic such as amoxicillin first-line. Nitrofurantoin should be avoided at term because of the risk of neonatal haemolysis

A 26-year-old man returns to the genito-urinary medicine clinic. He is a known intravenous drug user. Five days ago he was seen with a urethral discharge. A swab taken in the clinic showed a Gram-negative diplococcus and treatment with IM ceftriaxone was given. Unfortunately his symptoms have not resolved. What is the most likely explanation?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Gonorrhoea-resistant to ceftriaxone    |
| <input type="radio"/> | B. Co-existent <i>Candida</i> infection   |
| <input type="radio"/> | C. HIV infection                          |
| <input type="radio"/> | D. Co-existent syphilis infection         |
| <input type="radio"/> | E. Co-existent <i>Chlamydia</i> infection |

Next question

Co-existent infection with *Chlamydia* is extremely common in patients with gonorrhoea.

### **Chlamydia**

*Chlamydia* is the most prevalent sexually transmitted infection in the UK and is caused by *Chlamydia trachomatis*, an obligate intracellular pathogen. Approximately 1 in 10 young women in the UK have *Chlamydia*. The incubation period is around 7-21 days, although it should be remembered a large percentage of cases are asymptomatic

#### Features

- asymptomatic in around 70% of women and 50% of men
- women: cervicitis (discharge, bleeding), dysuria
- men: urethral discharge, dysuria

#### Potential complications

- epididymitis
- pelvic inflammatory disease
- endometritis
- increased incidence of ectopic pregnancies
- infertility
- reactive arthritis
- perihepatitis (Fitz-Hugh-Curtis syndrome)

#### Investigation

- traditional cell culture is no longer widely used
- nuclear acid amplification tests (NAATs) are now rapidly emerging as the investigation of choice

- urine (first void urine sample), vulvovaginal swab or cervical swab may be tested using the NAAT technique

## Screening

- in England the National *Chlamydia* Screening Programme is open to all men and women aged 15-24 years
- the 2009 SIGN guidelines support this approach, suggesting screening all sexually active patients aged 15-24 years
- relies heavily on opportunistic testing

## Management

- doxycycline (7 day course) or azithromycin (single dose). The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline
- if pregnant then erythromycin or amoxicillin may be used. The SIGN guidelines suggest considering azithromycin 'following discussion of the balance of benefits and risks with the patient'
- patients diagnosed with *Chlamydia* should be offered a choice of provider for initial partner notification - either trained practice nurses with support from GUM, or referral to GUM
- for men with symptomatic infection all partners from the four weeks prior to the onset of symptoms should be contacted
- for women and asymptomatic men all partners from the last six months or the most recent sexual partner should be contacted
- contacts of confirmed *Chlamydia* cases should be offered treatment prior to the results of their investigations being known (treat then test)



A pregnant 34-year-old female presents with uncomplicated Falciparum malaria following a trip to Kenya. Which one of the following is the most suitable treatment?

<input type="radio"/>	A. Chloroquine
<input type="radio"/>	B. Artemether-lumefantrine
<input type="radio"/>	C. Doxycycline
<input type="radio"/>	D. Quinine
<input type="radio"/>	E. Atovaquone-proguanil

Both artemether and atovaquone are not currently recommended in pregnancy

### Malaria: Falciparum

Feature of severe malaria

- schizonts on a blood film
- parasitaemia > 2%
- hypoglycaemia
- temperature > 39 °C
- severe anaemia
- complications as below

Complications

- cerebral malaria: seizures, coma
- acute renal failure: blackwater fever, secondary to intravascular haemolysis, mechanism unknown
- acute respiratory distress syndrome (ARDS)
- hypoglycaemia
- disseminated intravascular coagulation (DIC)

Uncomplicated falciparum malaria

- strains resistant to chloroquine are prevalent in certain areas of Asia and Africa
- the 2010 WHO guidelines recommend artemisinin-based combination therapies (ACTs) as first-line therapy
- examples include artemether plus lumefantrine, artesunate plus amodiaquine, artesunate plus mefloquine, artesunate plus sulfadoxine-pyrimethamine, dihydroartemisinin plus piperaquine

Severe falciparum malaria

- a parasite counts of more than 2% will usually need parenteral treatment irrespective of clinical state
- intravenous artesunate is now recommended by WHO in preference to intravenous quinine
- if parasite count > 10% then exchange transfusion should be considered
- shock may indicate coexistent bacterial septicaemia - malaria rarely causes haemodynamic collapse

Which one of the following features is not associated with Lyme disease?

<input type="radio"/>	A. Jarisch-Herxheimer reaction
<input type="radio"/>	B. Meningitis
<input type="radio"/>	C. Prolonged PR interval on ECG
<input type="radio"/>	D. Erythema marginatum
<input type="radio"/>	E. Arthralgia

Next question

Lyme disease is associated with erythema chronicum migrans

### Lyme disease: features

#### Early features

- erythema chronicum migrans (small papule often at site of the tick bite which develops into a larger annular lesion with central clearing, occurs in 70% of patients)
- systemic symptoms: malaise, fever, arthralgia

#### Later features

- CVS: heart block, myocarditis
- neurological: cranial nerve palsies, meningitis
- polyarthrititis

**Question 55 of 167**

Next

A 31-year-old woman is admitted to hospital. As part of a liver screen the following results are obtained:

Anti-HBs	Positive
Anti-HBc	Positive
HBs antigen	Negative

Anti-HBs = Hepatitis B Surface Antibody; Anti-HBc = Hepatitis B Core Antibody; HBs antigen = Hepatitis B Surface Antigen

What is the patient's hepatitis B status?

- ☐ A. Previous immunisation to hepatitis B
- ☐ B. Chronic hepatitis B - highly infectious
- ☐ C. Previous hepatitis B infection, not a carrier
- ☐ D. Chronic hepatitis B - not infectious
- ☐ E. Acute hepatitis B infection

[Next question](#)**Hepatitis B serology**

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months. IgG anti-HBc persists
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

**Example results**

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

Which of the following is true regarding the *Salmonella* species?

<input type="radio"/>	A. Rose spots appear in all patients with typhoid
<input type="radio"/>	B. They are normally present in the gut as commensals
<input type="radio"/>	C. They are anaerobic organisms
<input type="radio"/>	D. A relative bradycardia is often seen in typhoid fever
<input type="radio"/>	E. <i>Salmonella typhi</i> can be categorised into type A, B and C

Next question

### **Salmonella**

The *Salmonella* group contains many members, most of which cause diarrhoeal diseases. They are aerobic, Gram negative rods which are not normally present as commensals in the gut.

Typhoid and paratyphoid are caused by *Salmonella typhi* and *Salmonella paratyphi* (types A, B & C) respectively. They are often termed enteric fevers, producing systemic symptoms such as headache, fever, arthralgia

#### Features

- initially systemic upset as above
- relative bradycardia
- abdominal pain, distension
- constipation: although *Salmonella* is a recognised cause of diarrhoea, constipation is more common in typhoid
- rose spots: present on the trunk in 40% of patients, and are more common in paratyphoid

#### Possible complications include

- osteomyelitis (especially in sickle cell disease where *Salmonella* is one of the most common pathogens)
- GI bleed/perforation
- meningitis
- cholecystitis
- chronic carriage (1%, more likely if adult females)

Which one of the following is true regarding *Escherichia coli* infection?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. It is a Gram negative coccus                         |
| <input type="radio"/> | B. E coli is an important cause of neonatal meningitis  |
| <input type="radio"/> | C. The O157:H7 strain is typically spread via shellfish |
| <input type="radio"/> | D. Severe infection should be treated with teicoplanin  |
| <input type="radio"/> | E. It is an aerobic bacteria                            |

Next question

*Escherichia coli* is classified as a facultative anaerobe

### ***Escherichia coli***

*Escherichia coli* is a facultative anaerobic, lactose-fermenting, Gram negative rod which is a normal gut commensal.

E coli infections lead to a variety of diseases in humans including:

- diarrhoeal illnesses
- UTIs
- neonatal meningitis

E coli O157:H7 is a particular strain associated with severe, haemorrhagic, watery diarrhoea. It has a high mortality rate and can be complicated by haemolytic uraemic syndrome. It is often spread by contaminated ground beef.

**Question 58 of 167**

Next

A 34-year-old man presents with a widespread maculopapular rash and mouth ulcers. Two months ago he presented to the local GUM clinic after developing a painless penile ulcer. At the time he was noted to have inguinal lymphadenopathy. Which one of the following organisms is most likely to be responsible?

<input type="radio"/>	A. Lymphogranuloma venereum
<input type="radio"/>	B. Herpes simplex virus type 2
<input type="radio"/>	C. <i>Mycoplasma genitalium</i>
<input type="radio"/>	D. <i>Haemophilus ducreyi</i>
<input type="radio"/>	E. <i>Treponema pallidum</i>

Next question

This patient has symptoms of secondary syphilis.

**Syphilis**

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*. Infection is characterised by primary, secondary and tertiary stages. The incubation period is between 9-90 days

**Primary features**

- chancre - painless ulcer at the site of sexual contact
- local lymphadenopathy
- often not seen in women (the lesion may be on the cervix)

Secondary features - occurs 6-10 weeks after primary infection

- systemic symptoms: fevers, lymphadenopathy
- rash on trunk, palms and soles
- buccal 'snail track' ulcers (30%)
- condylomata lata

**Latent period****Tertiary features**

- gummas
- aortic aneurysms
- general paralysis of the insane
- tabes dorsalis

A 34-year-old HIV positive man is being treated for *Pneumocystis carinii* pneumonia with co-trimoxazole. Arterial blood gases show a pO<sub>2</sub> of 8.2 kPa. What drug should be added to treatment?

<input type="radio"/>	A. Meropenem
<input type="radio"/>	B. Chloramphenicol
<input type="radio"/>	C. Steroids
<input type="radio"/>	D. Nebulised fluconazole
<input type="radio"/>	E. Magnesium sulphate

[Next question](#)

### HIV: *Pneumocystis jiroveci* pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as *Pneumocystis jiroveci*, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- *Pneumocystis jiroveci* is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count < 200/mm<sup>3</sup> should receive PCP prophylaxis

#### Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Extrapulmonary manifestations are rare (1-2% of cases), may cause

- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

#### Investigation

- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal
- exercise-induced desaturation

- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain)

## Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if  $pO_2 < 9.3\text{kPa}$  then steroids reduce risk of respiratory failure by 50% and death by a third)



What is the mechanism of action of the antiviral agent ribavirin?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Inhibits DNA polymerase                             |
| <input type="radio"/> | B. Inhibits uncoating of virus in the cell             |
| <input type="radio"/> | C. Protease inhibitor                                  |
| <input type="radio"/> | D. Nucleoside analogue reverse transcriptase inhibitor |
| <input type="radio"/> | E. Interferes with the capping of viral mRNA           |

Next question

## Antiviral agents

### Aciclovir

- aciclovir is phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase

### Ribavirin

- effective against a range of DNA and RNA viruses
- interferes with the capping of viral mRNA

### Interferons

- inhibit synthesis of mRNA, translation of viral proteins, viral assembly and release

### Amantadine

- used to treat influenza
- inhibits uncoating of virus in cell

## Anti-retroviral agent used in HIV

### Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine

### Protease inhibitors (PI)

- inhibits a protease needed to make the virus able to survive outside the cell
- examples: indinavir, nelfinavir, ritonavir, saquinavir

#### Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz

Which of the following anti-retroviral drugs is most characteristically associated with nephrolithiasis?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Zidovudine |
| <input type="radio"/> | B. Didanosine |
| <input type="radio"/> | C. Indinavir  |
| <input type="radio"/> | D. Ritonavir  |
| <input type="radio"/> | E. Nevirapine |

Next question

### HIV: anti-retrovirals

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

Protease inhibitors (PI)

- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system

**Question 62 of 167**

Next

Each of the following organisms commonly cause respiratory tract infections in patients with cystic fibrosis, except:

<input type="radio"/>	A. Aspergillus
<input type="radio"/>	B. <i>Pseudomonas aeruginosa</i>
<input type="radio"/>	C. <i>Burkholderia cepacia</i>
<input type="radio"/>	D. Staphylococcal aureus
<input type="radio"/>	E. <i>Strongyloides stercoralis</i>

Next question

**Cystic fibrosis**

Cystic fibrosis (CF) is an autosomal recessive disorder causing increased viscosity of secretions (e.g. lungs and pancreas). It is due to a defect in the cystic fibrosis transmembrane conductance regulator gene (CFTR), which codes a cAMP-regulated chloride channel

In the UK 80% of CF cases are due to delta F508 on the long arm of chromosome 7. Cystic fibrosis affects 1 per 2500 births, and the carrier rate is c. 1 in 25

Organisms which may colonise CF patients

- Staph aureus
- *Pseudomonas aeruginosa*
- *Burkholderia cepacia*\*
- Aspergillus

\*previously known as *Pseudomonas cepacia*

A 30-year-old man comes for review. He returned from a holiday in Egypt yesterday. For the past two days he has been passing frequent bloody diarrhoea associated with crampy abdominal pain. Abdominal examination demonstrates diffuse lower abdominal tenderness but there is no guarding or rigidity. His temperature is 37.5°C. What is the most likely causative organism?

- ☐ A. Giardiasis
- ☐ B. Enterotoxigenic *Escherichia coli*
- ☐ C. *Staphylococcus aureus*
- ☐ D. *Salmonella*
- ☐ E. *Shigella*

[Next question](#)

Enterotoxigenic *Escherichia coli* infections do not usually cause bloody diarrhoea. A differential diagnosis would be amoebic dysentery, enterohemorrhagic *Escherichia coli* and possibly *Campylobacter*.

## Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

## Stereotypical histories

<b><i>Escherichia coli</i></b>	Common amongst travellers Watery stools Abdominal cramps and nausea
<b>Giardiasis</b>	Prolonged, non-bloody diarrhoea
<b>Cholera</b>	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
<b><i>Shigella</i></b>	Bloody diarrhoea Vomiting and abdominal pain
<b><i>Staphylococcus aureus</i></b>	Severe vomiting Short incubation period
<b><i>Campylobacter</i></b>	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody  Complications include Guillain-Barre syndrome

<b><i>Bacillus cereus</i></b>	Two types of illness are seen <ul style="list-style-type: none"> <li>• vomiting within 6 hours, stereotypically due to rice</li> <li>• diarrhoeal illness occurring after 6 hours</li> </ul>
<b>Amoebiasis</b>	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

#### Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus*\*
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

\*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

A 45-year-old man is diagnosed as having primary syphilis. Six hours after receiving his first injection of benzylpenicillin he complains of feeling generally unwell. On examination he appears flushed. His blood pressure is 94/62 mmHg, pulse 96/min and temperature 37.9°. These symptoms settle after around four hours. Which one of the following is most likely to explain this finding.

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Arunan-Leadbetter reaction                    |
| <input type="radio"/> | B. Jarisch-Herxheimer reaction                   |
| <input type="radio"/> | C. Concurrent infectious mononucleosis infection |
| <input type="radio"/> | D. Allergic reaction to benzylpenicillin         |
| <input type="radio"/> | E. Undiagnosed tertiary syphilis                 |

[Next question](#)

## Syphilis: management

### Management

- benzylpenicillin
- alternatives: doxycycline
- the Jarisch-Herxheimer reaction is sometimes seen following treatment. Fever, rash, tachycardia after first dose of antibiotic. It is thought to be due to the release of endotoxins following bacterial death and typically occurs within a few hours of treatment.

Which one of the following is least likely to cause a pyrexia of unknown origin?

<input type="radio"/>	A. Hypernephroma
<input type="radio"/>	B. Colorectal cancer
<input type="radio"/>	C. Lymphoma
<input type="radio"/>	D. Atrial myxoma
<input type="radio"/>	E. Tuberculosis

Next question

Very rarely colorectal cancer may cause endocarditis secondary to *Streptococcus bovis*, but this is the least likely of the options

### Pyrexia of unknown origin

Defined as a prolonged fever of > 3 weeks which resists diagnosis after a week in hospital

#### Neoplasia

- lymphoma
- hypernephroma
- preleukaemia
- atrial myxoma

#### Infections

- abscess
- TB

#### Connective tissue disorders



Which one of the following is the most common cause of visceral larva migrans?

<input type="radio"/>	A. <i>Cryptococcus neoformans</i>
<input type="radio"/>	B. <i>Strongyloides stercoralis</i>
<input type="radio"/>	C. Visceral leishmaniasis
<input type="radio"/>	D. <i>Toxocara canis</i>
<input type="radio"/>	E. Giardiasis

Next question

## Nematodes

### Ancylostoma braziliense

- most common cause of cutaneous larva migrans
- common in Central and Southern America

### Strongyloides stercoralis

- acquired percutaneously (e.g. walking barefoot)
- causes pruritus and larva currens - this has a similar appearance to cutaneous larva migrans but moves through the skin at a far greater rate
- abdo pain, diarrhoea, pneumonitis
- may cause Gram negative septicaemia due carrying of bacteria into bloodstream
- eosinophilia sometimes seen
- management: thiabendazole, albendazole. Ivermectin also used, particularly in chronic infections

### Toxocara canis

- commonly acquired by ingesting eggs from soil contaminated by dog faeces
- commonest cause of visceral larva migrans
- other features: eye granulomas, liver/lung involvement

A 7-year-old male presents with generalised lymphadenopathy. Which one of the following is least likely to result in this presentation?

<input type="radio"/>	A. Kawasaki disease
<input type="radio"/>	B. Cytomegalovirus
<input type="radio"/>	C. Acute lymphoblastic leukaemia
<input type="radio"/>	D. Phenytoin therapy
<input type="radio"/>	E. Infectious mononucleosis

[Next question](#)

Kawasaki disease causes only cervical lymphadenopathy

### Lymphadenopathy

There are many causes of generalised lymphadenopathy

#### Infective

- infectious mononucleosis
- HIV, including seroconversion illness
- eczema with secondary infection
- rubella
- toxoplasmosis
- CMV
- tuberculosis
- roseola infantum

#### Neoplastic

- leukaemia
- lymphoma

#### Others

- autoimmune conditions: SLE, rheumatoid arthritis
- graft versus host disease
- sarcoidosis
- drugs: phenytoin and to a lesser extent allopurinol, isoniazid

A 23-year-old male presents with a purulent urethral discharge. A sample of the discharge is shown to be a Gram negative diplococcus. What is the most appropriate antimicrobial therapy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Ciprofloxacin 500mg BD PO for 7 days |
| <input type="radio"/> | B. Penicillin V 500mg QDS PO for 7 days |
| <input type="radio"/> | C. Doxycycline 100mg BD PO for 7 days   |
| <input type="radio"/> | D. Ciprofloxacin 500mg PO (single dose) |
| <input type="radio"/> | E. Cefixime 400mg PO (single dose)      |

[Next question](#)

Cephalosporins are now the treatment of choice for Gonorrhoea

Ciprofloxacin should only be used if the organism is known to be sensitive due to increasing resistance. Penicillin, previously first-line treatment, is rarely used now due to widespread resistance

### Gonorrhoea

Gonorrhoea is caused by the Gram negative diplococcus *Neisseria gonorrhoea*. Acute infection can occur on any mucous membrane surface, typically genitourinary but also rectum and pharynx. The incubation period of gonorrhoea is 2-5 days

#### Features

- males: urethral discharge, dysuria
- females: cervicitis e.g. leading to vaginal discharge
- rectal and pharyngeal infection is usually asymptomatic

Local complications that may develop include urethral strictures, epididymitis and salpingitis (hence may lead to infertility). Disseminated infection may occur - see below

#### Management

- ciprofloxacin 500mg PO used to be the treatment of choice
- however, there is increased resistance to ciprofloxacin and therefore cephalosporins are now used
- options include cefixime 400mg PO (single dose) or ceftriaxone 250mg IM

Disseminated gonococcal infection (DGI) and gonococcal arthritis may also occur, with gonococcal infection being the most common cause of septic arthritis in young adults. The pathophysiology of DGI is not fully understood but is thought to be due to haematogenous spread from mucosal infection (e.g. Asymptomatic genital

infection). Initially there may be a classic triad of symptoms: tenosynovitis, migratory polyarthrititis and dermatitis. Later complications include septic arthritis, endocarditis and perihepatitis (Fitz-Hugh-Curtis syndrome)

Key features of disseminated gonococcal infection

- tenosynovitis
- migratory polyarthrititis
- dermatitis (lesions can be maculopapular or vesicular)

A 43-year-old man from Sierra Leone presents with a flu-like illness. On examination he has very large posterior cervical lymph nodes. A diagnosis of African trypanosomiasis is confirmed on blood smear. What is the most appropriate treatment?

<input type="radio"/>	A. Atovaquone-proguanil
<input type="radio"/>	B. Sodium stibogluconate
<input type="radio"/>	C. Benznidazole
<input type="radio"/>	D. Metronidazole
<input type="radio"/>	E. Pentamidine

[Next question](#)

### Trypanosomiasis

Two main form of this protozoal disease are recognised - African trypanosomiasis (sleeping sickness) and American trypanosomiasis (Chagas' disease)

Two forms of **African trypanosomiasis**, or **sleeping sickness**, are seen - *Trypanosoma gambiense* in West Africa and *Trypanosoma rhodesiense* in East Africa. Both types are spread by the tsetse fly. *Trypanosoma rhodesiense* tends to follow a more acute course. Clinical features include:

- Trypanosoma chancre - tender subcutaneous nodule at site of infection
- enlargement of posterior cervical lymph nodes
- later: central nervous system involvement e.g. meningoencephalitis

#### Management

- early disease: IV pentamidine or suramin
- later disease or central nervous system involvement: IV melarsoprol

**American trypanosomiasis**, or **Chagas' disease**, is caused by the protozoan *Trypanosoma cruzi*. The vast majority of patients (95%) are asymptomatic in the acute phase although a chagoma (an erythematous nodule at site of infection) and periorbital oedema are sometimes seen. Chronic Chagas' disease mainly affects the heart and gastrointestinal tract

- myocarditis may lead to heart failure and arrhythmias
- gastrointestinal features includes megaoesophagus and megacolon causing dysphagia and constipation

#### Management

- treatment is most effective in the acute phase using azole or nitroderivatives such as benznidazole or nifurtimox
- chronic disease management involves treating the complications e.g., heart failure

A 39-year-old man with HIV is admitted due to shortness of breath. Chest x-ray shows bilateral pulmonary infiltrates and *Pneumocystis carinii* pneumonia is suspected. What type of staining should be applied to the bronchoalveolar lavage to demonstrate the organism?

<input type="radio"/>	A. Rubeanic acid
<input type="radio"/>	B. Silver stain
<input type="radio"/>	C. Pearl's stain
<input type="radio"/>	D. Rose Bengal
<input type="radio"/>	E. Congo red

[Next question](#)

### HIV: *Pneumocystis jiroveci* pneumonia

Whilst the organism *Pneumocystis carinii* is now referred to as *Pneumocystis jiroveci*, the term *Pneumocystis carinii* pneumonia (PCP) is still in common use

- *Pneumocystis jiroveci* is an unicellular eukaryote, generally classified as a fungus but some authorities consider it a protozoa
- PCP is the most common opportunistic infection in AIDS
- all patients with a CD4 count < 200/mm<sup>3</sup> should receive PCP prophylaxis

#### Features

- dyspnoea
- dry cough
- fever
- very few chest signs

Extrapulmonary manifestations are rare (1-2% of cases), may cause

- hepatosplenomegaly
- lymphadenopathy
- choroid lesions

#### Investigation

- CXR: typically shows bilateral interstitial pulmonary infiltrates but can present with other x-ray findings e.g. lobar consolidation. May be normal

- exercise-induced desaturation
- sputum often fails to show PCP, bronchoalveolar lavage (BAL) often needed to demonstrate PCP (silver stain)

## Management

- co-trimoxazole
- IV pentamidine in severe cases
- steroids if hypoxic (if  $pO_2 < 9.3\text{kPa}$  then steroids reduce risk of respiratory failure by 50% and death by a third)

**Question 71 of 167**

Next

A 77-year-old female presents with a non-healing ulcer on her right foot. Blood cultures grow MRSA. Which antibiotic would you consider in addition to vancomycin?

<input type="radio"/>	A. Flucloxacillin
<input type="radio"/>	B. Ceftazidime
<input type="radio"/>	C. Ciprofloxacin
<input type="radio"/>	D. Metronidazole
<input type="radio"/>	E. Rifampicin

Next question

**MRSA**

Methicillin-resistant *Staphylococcus aureus* (MRSA) was one of the first organisms which highlighted the dangers of hospital-acquired infections.

Who should be screened for MRSA?

- all patients awaiting elective admissions (exceptions include day patients having terminations of pregnancy and ophthalmic surgery. Patients admitted to mental health trusts are also excluded)
- from 2011 all emergency admissions will be screened

How should a patient be screened for MRSA?

- nasal swab and skin lesions or wounds
- the swab should be wiped around the inside rim of a patient's nose for 5 seconds
- the microbiology form must be labelled 'MRSA screen'

Suppression of MRSA from a carrier once identified

- nose: mupirocin 2% in white soft paraffin, tds for 5 days
- skin: chlorhexidine gluconate, od for 5 days. Apply all over but particularly to the axilla, groin and perineum

The following antibiotics are commonly used in the treatment of MRSA infections:

- vancomycin
- teicoplanin



Some strains may be sensitive to the antibiotics listed below but they should not generally be used alone because resistance may develop:

- rifampicin
- macrolides
- tetracyclines
- aminoglycosides
- clindamycin

Relatively new antibiotics such as linezolid, quinupristin/dalfopristin combinations and tigecycline have activity against MRSA but should be reserved for resistant cases

Which one of the following vaccines uses an extract of the organism or virus?

<input type="radio"/>	A. Rabies
<input type="radio"/>	B. Yellow fever
<input type="radio"/>	C. Oral polio
<input type="radio"/>	D. Measles
<input type="radio"/>	E. Meningococcus

Next question

## Vaccinations

It is important to be aware of vaccines which are of the live-attenuated type as these may pose a risk to immunocompromised patients. The main types of vaccine are as follows:

### Live attenuated

- BCG
- measles, mumps, rubella (MMR)
- oral polio
- yellow fever
- oral typhoid\*

### Inactivated preparations

- rabies
- influenza

### Detoxified exotoxins

- tetanus

### Extracts of the organism/virus (sometimes termed fragment)\*\*

- diphtheria
- pertussis ('acellular' vaccine)
- hepatitis B
- meningococcus, pneumococcus, haemophilus

## Notes

- influenza: different types are available, including whole inactivated virus, split virion (virus particles disrupted by detergent treatment) and sub-unit (mainly haemagglutinin and neuraminidase)
- cholera: contains inactivated Inaba and Ogawa strains of *Vibrio cholerae* together with recombinant B-subunit of the cholera toxin
- hepatitis B: contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology

\*whole cell typhoid vaccine is no longer used in the UK

\*\*may also be produced using recombinant DNA technology

**Question 73 of 167**

Next

A woman who is 14 weeks pregnant presents as she came into contact with a child who has chickenpox around 4 days ago. She is unsure if she had the condition herself as a child. Blood tests show the following:

Varicella IgM	Negative
Varicella IgG	Negative

What is the most appropriate management?

- ☐ A. Varicella zoster immunoglobulin
- ☐ B. No action required
- ☐ C. IV aciclovir
- ☐ D. Varicella zoster vaccination
- ☐ E. Varicella zoster vaccination + varicella zoster immunoglobulin

Next question

Chickenpox exposure when pregnant - if not immune give VZIG

The negative IgG indicates no previous exposure to chickenpox

**Chickenpox exposure in pregnancy**

Chickenpox is caused by primary infection with varicella zoster virus. Shingles is reactivation of dormant virus in dorsal root ganglion. In pregnancy there is a risk to both the mother and also the fetus, a syndrome now termed fetal varicella syndrome

Fetal varicella syndrome (FVS)

- risk of FVS following maternal varicella exposure is around 1% if occurs before 20 weeks gestation
- studies have shown a very small number of cases occurring between 20-28 weeks gestation and none following 28 weeks
- features of FVS include skin scarring, eye defects (microphthalmia), limb hypoplasia, microcephaly and learning disabilities

Management of chickenpox exposure

- if there is any doubt about the mother previously having chickenpox maternal blood should be checked for varicella antibodies
- if the pregnant woman is not immune to varicella she should be given varicella zoster immunoglobulin (VZIG) as soon as possible. RCOG and Greenbook guidelines suggest VZIG is effective up to 10 days post exposure

- consensus guidelines suggest oral aciclovir should be given if pregnant women with chickenpox present within 24 hours of onset of the rash

Which of the following infections usually has the longest incubation period?

<input type="radio"/>	A. Meningococcus
<input type="radio"/>	B. Scarlet fever
<input type="radio"/>	C. Typhoid
<input type="radio"/>	D. Diphtheria
<input type="radio"/>	E. Influenza

[Next question](#)

### Incubation periods

Questions may either ask directly about incubation periods or they may be used to provide a clue in a differential diagnosis

Less than 1 week

- meningococcus
- diphtheria
- influenza
- scarlet fever

1 - 2 weeks

- malaria
- dengue fever
- typhoid
- measles

2 - 3 weeks

- mumps
- rubella
- chickenpox

Longer than 3 weeks

- infectious mononucleosis
- cytomegalovirus
- viral hepatitis
- HIV

A 14-year-old boy presents with pyrexia, myalgia and lethargy. Clinical examination reveals a temperature of 38.8°C. He is haemodynamically stable and his chest is clear. Given the current pandemic a presumptive diagnosis of H1N1 influenza is made and oseltamivir is prescribed. What is the most likely side-effect he will experience?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Dry mouth    |
| <input type="radio"/> | B. Headache     |
| <input type="radio"/> | C. Bronchospasm |
| <input type="radio"/> | D. Nausea       |
| <input type="radio"/> | E. Rash         |

[Next question](#)

Gastrointestinal symptoms are the most common side-effects of oseltamivir (Tamiflu).

### H1N1 influenza pandemic

The 2009 H1N1 influenza (swine flu) outbreak was first observed in Mexico in early 2009. In June 2009, the WHO declared the outbreak to be a pandemic.

#### H1N1

The H1N1 virus is a subtype of the influenza A virus and the most common cause of flu in humans. The 2009 pandemic was caused by a new strain of the H1N1 virus.

The following groups are particularly at risk:

- patients with chronic illnesses and those on immunosuppressants
- pregnant women
- young children under 5 years old

#### Features

The majority of symptoms are typical of those seen in a flu-like illness:

- fever greater than 38°C
- myalgia
- lethargy
- headache
- rhinitis
- sore throat
- cough
- diarrhoea and vomiting

A minority of patients may go on to develop an acute respiratory distress syndrome which may require ventilatory support.

## **Treatment**

There are two main treatments currently available:

### Oseltamivir (Tamiflu)

- oral medication
- a neuraminidase inhibitor which prevents new viral particles from being released by infected cells
- common side-effects include nausea, vomiting, diarrhoea and headaches

### Zanamivir (Relenza)

- inhaled medication\*
- also a neuraminidase inhibitor
- may induce bronchospasm in asthmatics

\*intravenous preparations are available for patients who are acutely unwell



Which one of the following antibiotics is most likely to cause pseudomembranous colitis?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Cefuroxime              |
| <input type="radio"/> | B. Cefalexin               |
| <input type="radio"/> | C. Ciprofloxacin           |
| <input type="radio"/> | D. Co-amoxiclav            |
| <input type="radio"/> | E. Piperacillin-tazobactam |

Next question

Cephalosporins, not just clindamycin, are strongly linked to *Clostridium difficile*

This is a difficult question as both co-amoxiclav and ciprofloxacin are known to cause *Clostridium difficile*. Studies looking at the relative risk (RR) of developing *Clostridium difficile* following antibiotic therapy give the following results (please see the link):

- clindamycin: RR = 31.8
- cephalosporins: RR = 14.9
- ciprofloxacin: RR = 5.0

Cefalexin is a first generation cephalosporin and less associated with *Clostridium difficile* than newer agents such as ceftriaxone

### ***Clostridium difficile***

*Clostridium difficile* is a Gram positive rod often encountered in hospital practice. It produces an exotoxin which causes intestinal damage leading to a syndrome called pseudomembranous colitis. *Clostridium difficile* develops when the normal gut flora are suppressed by broad-spectrum antibiotics. Clindamycin is historically associated with causing *Clostridium difficile* but the aetiology has evolved significantly over the past 10 years. Second and third generation cephalosporins are now the leading cause of *Clostridium difficile*.

#### Features

- diarrhoea
- abdominal pain
- a raised white blood cell count is characteristic
- if severe toxic megacolon may develop

Diagnosis is made by detecting *Clostridium difficile* toxin (CDT) in the stool

## Management

- first-line therapy is oral metronidazole for 10-14 days
- if severe or not responding to metronidazole then oral vancomycin may be used
- for life-threatening infections a combination of oral vancomycin and intravenous metronidazole should be used

A 53-year-old woman is diagnosed with left leg cellulitis. A swab is taken and oral flucloxacillin is started. The following result is obtained:

Skin swab:	Group A <i>Streptococcus</i>
------------	------------------------------

How should the antibiotic therapy be changed?

<input type="radio"/>	A. No change
<input type="radio"/>	B. Add topical fusidic acid
<input type="radio"/>	C. Add clindamycin
<input type="radio"/>	D. Switch to phenoxymethylpenicillin
<input type="radio"/>	E. Add erythromycin

Next question

Penicillin is the antibiotic of choice for group A streptococcal infections. The BNF suggests stopping flucloxacillin if streptococcal infection is confirmed in patients with cellulitis, due to the high sensitivity. This should be balanced however with the variable absorption of phenoxymethylpenicillin.

## Streptococci

Streptococci are gram-positive cocci. They may be divided into alpha and beta haemolytic types

### Alpha haemolytic streptococci (partial haemolysis)

The most important alpha haemolytic *Streptococcus* is *Streptococcus pneumoniae* (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is *Streptococcus viridans*

### Beta haemolytic streptococci (complete haemolysis)

These can be subdivided into groups A-H. Only groups A, B & D are important in humans.

#### Group A

- most important organism is *Streptococcus pyogenes*
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

#### Group B

- *Streptococcus agalactiae* may lead to neonatal meningitis and septicaemia

## Group D

- *Enterococcus*

**Question 78 of 167**

Next

A 55-year-old business man presents with a 15 day history of watery, non-bloody diarrhoea associated with anorexia and abdominal bloating. His symptoms started 4 days after returning from a trip to Pakistan. On examination he is afebrile with dry mucous membranes but normal skin turgor. Given the likely organism, what is the most appropriate treatment?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Hydroxychloroquine |
| <input type="radio"/> | B. Aciclovir          |
| <input type="radio"/> | C. Benzylpenicillin   |
| <input type="radio"/> | D. Ciprofloxacin      |
| <input type="radio"/> | E. Metronidazole      |

Next question

Although *Escherichia coli* is the most common cause of travellers' diarrhoea, in this particular case the length of illness and nature of symptoms (bloating, watery diarrhoea) points to a diagnosis of Giardiasis.

**Giardiasis**

Giardiasis is caused by the flagellate protozoan *Giardia lamblia*. It is spread by the faeco-oral route

**Features**

- often asymptomatic
- lethargy, bloating, abdominal pain
- non-bloody diarrhoea
- chronic diarrhoea, malabsorption and lactose intolerance can occur
- stool microscopy for trophozoite and cysts are classically negative, therefore duodenal fluid aspirates or 'string tests' (fluid absorbed onto swallowed string) are sometimes needed

Treatment is with metronidazole

A 30-year-old man presents for review two weeks after returning from a camping holiday in the New Forest. For the past few days he has felt general unwell with lethargy and arthralgia. On examination he has a rash consistent with erythema chronicum migrans. What is the most appropriate test to perform given the likely diagnosis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. ELISA test for antibodies to <i>Borrelia burgdorferi</i> |
| <input type="radio"/> | B. Polymerase chain reaction for <i>Borrelia</i> DNA        |
| <input type="radio"/> | C. Blood cultures   |
| <input type="radio"/> | D. Blood film   |
| <input type="radio"/> | E. Bone marrow biopsy                                       |

[Next question](#)

Serological tests are the most appropriate first line investigation for diagnosing Lyme disease. ELISA tests are preferred to Western blots as they are more sensitive.

## Lyme disease

Lyme disease is caused by the spirochaete *Borrelia burgdorferi* and is spread by ticks

### Features

- early: erythema chronicum migrans + systemic features (fever, arthralgia)
- CVS: heart block, myocarditis
- neuro: cranial nerve palsies, meningitis

### Investigation

- serology: antibodies to *Borrelia burgdorferi*

### Management

- doxycycline if early disease
- ceftriaxone if disseminated disease
- Jarisch-Herxheimer reaction is sometimes seen after initiating therapy: fever, rash, tachycardia after first dose of antibiotic (more commonly seen in syphilis, another spirochaetal disease)

What is the mechanism of action of macrolides?

<input type="radio"/>	A. Causes misreading of mRNA
<input type="radio"/>	B. Interferes with cell wall formation
<input type="radio"/>	C. Inhibits DNA synthesis
<input type="radio"/>	D. Inhibits RNA synthesis
<input type="radio"/>	E. Inhibits protein synthesis

Next question

### Antibiotics: mechanisms of action

The lists below summarise the site of action of the commonly used antibiotics

Inhibit cell wall formation

- penicillins
- cephalosporins

Inhibit protein synthesis

- aminoglycosides (cause misreading of mRNA)
- chloramphenicol
- macrolides (e.g. erythromycin)
- tetracyclines
- fusidic acid

Inhibit DNA synthesis

- quinolones (e.g. ciprofloxacin)
- metronidazole
- sulphonamides
- trimethoprim

Inhibit RNA synthesis

- rifampicin

A 34-year-old abattoir worker presents to the Emergency Department following the development of black skin lesions. On examination a black eschar is noted with extensive surrounding oedema. A diagnosis of cutaneous anthrax is suspected. What is the most appropriate initial antibiotic therapy until sensitivities are known?

<input type="radio"/>	A. Ciprofloxacin
<input type="radio"/>	B. Metronidazole
<input type="radio"/>	C. Erythromycin
<input type="radio"/>	D. Benzylpenicillin
<input type="radio"/>	E. Gentamicin

[Next question](#)

The current Health Protection Agency advice for the initial management of cutaneous anthrax is ciprofloxacin

### Anthrax

Anthrax is caused by *Bacillus anthracis*, a Gram positive rod. It is spread by infected carcasses. It is also known as Woolsorters' disease. *Bacillus anthracis* produces a tripartite protein toxin

- protective antigen
- oedema factor: increases cAMP
- lethal factor: toxic to macrophages

### Features

- causes painless black eschar (cutaneous 'malignant pustule', but no pus)
- typically painless and non-tender
- may cause marked oedema
- anthrax can cause gastrointestinal bleeding

### Management

- the current Health Protection Agency advice for the initial management of cutaneous anthrax is ciprofloxacin
- further treatment is based on microbiological investigations and expert advice



A 23-year-old man has a Mantoux test prior to receiving the BCG vaccine. He develops a 12 mm indurated lesion on his forearm. Which one of the following cytokines is most involved in this response?

- ☐ A. Interleukin-8
- ☐ B. Interferon- $\gamma$
- ☐ C. Interferon- $\beta$
- ☐ D. Interferon- $\alpha$
- ☐ E. Interleukin-10

[Next question](#)

Tuberculin skin tests are an example of type IV (delayed) hypersensitivity reactions. These are largely mediated by interferon- $\gamma$  secreted by  $T_H1$  cells which in turn stimulates macrophage activity.

### Tuberculosis: screening

The Mantoux test is the main technique used to screen for latent tuberculosis. In recent years the interferon-gamma blood test has also been introduced. It is used in a number of specific situations such as:

- the Mantoux test is positive or equivocal
- people where a tuberculin test may be falsely negative (see below)

### Mantoux test

- 0.1 ml of 1:1,000 purified protein derivative (PPD) injected intradermally
- result read 2-3 days later

Diameter of induration	Positivity	Interpretation
< 6mm	Negative - no significant hypersensitivity to tuberculin protein	Previously unvaccinated individuals may be given the BCG
6 - 15mm	Positive - hypersensitive to tuberculin protein	Should not be given BCG. May be due to previous TB infection or BCG
> 15mm	Strongly positive - strongly hypersensitive to tuberculin protein	Suggests tuberculosis infection.

False negative tests may be caused by:

- miliary TB
- sarcoidosis
- HIV
- lymphoma

- very young age (e.g. < 6 months)

### **Heaf test**

The Heaf test was previously used in the UK but has been since been discontinued. It involved injection of PPD equivalent to 100,000 units per ml to the skin over the flexor surface of the left forearm. It was then read 3-10 days later.

Which one of the following is a Gram positive coccus?

<input type="radio"/>	A. <i>Enterococcus faecalis</i>
<input type="radio"/>	B. <i>Moraxella catarrhalis</i>
<input type="radio"/>	C. <i>Haemophilus influenzae</i>
<input type="radio"/>	D. <i>Neisseria meningitidis</i>
<input type="radio"/>	E. <i>Bacillus anthracis</i>

Next question

### Classification of bacteria

Remember:

- Gram positive cocci = staphylococci + streptococci (including enterococci)
- Gram negative cocci = *Neisseria meningitidis* + *Neisseria gonorrhoeae*, also *Moraxella*

Therefore, only a small list of Gram positive rods (bacilli) need to be memorised to categorise all bacteria -  
mnemonic = ABCD L

- *Actinomyces*
- *Bacillus anthracis* (anthrax)
- *Clostridium*
- Diphtheria: *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

Remaining organisms are Gram negative rods

A 25-year-old man with a history of epilepsy presents for advice regarding malarial prophylaxis. Next month he plans to travel to Vietnam. His trip will take him to some of the costal tourist destinations but he also plans to travel inland. What is the most appropriate medication to prevent him developing malaria?

- ☐ A. Quinine
- ☐ B. Atovaquone + proguanil
- ☐ C. Mefloquine
- ☐ D. Primaquine
- ☐ E. Pyrimethamine + sulfadoxine

Next question

In certain parts of South-East Asia there is widespread chloroquine resistance. Chemoprophylaxis using atovaquone + proguanil (Malarone), mefloquine (Lariam) or doxycycline is therefore recommended. Mefloquine should be avoided in this patient due to his history of epilepsy.

### Malaria: prophylaxis

There are around 1,500-2,000 cases each year of malaria in patients returning from endemic countries. The majority of these cases (around 75%) are caused by the potentially fatal *Plasmodium falciparum* protozoa. The majority of patients who develop malaria did not take prophylaxis. It should also be remembered that UK citizens who originate from malaria endemic areas quickly lose their innate immunity.

Up-to-date charts with recommended regimes for malarial zones should be consulted prior to prescribing

Drug	Side-effects + notes	Time to begin before travel	Time to end after travel
Atovaquone + proguanil (Malarone)	GI upset	1 - 2 days	7 days
Chloroquine	Headache Contraindicated in epilepsy Taken weekly	1 week	4 weeks
Doxycycline	Photosensitivity Oesophagitis	1 - 2 days	4 weeks
Mefloquine (Lariam)	Dizziness Neuropsychiatric disturbance Contraindicated in epilepsy Taken weekly	2 - 3 weeks	4 weeks
Proguanil (Paludrine)		1 week	4 weeks
Proguanil + chloroquine	See above	1 week	4 weeks

Pregnant women should be advised to avoid travelling to regions where malaria is endemic. Diagnosis can also

be difficult as parasites may not be detectable in the blood film due to placental sequestration. However, if travel cannot be avoided:

- chloroquine can be taken
- proguanil: folate supplementation (5mg od) should be given
- Malarone (atovaquone + proguanil): the BNF advises to avoid these drugs unless essential. If taken then folate supplementation should be given
- mefloquine: caution advised
- doxycycline is contraindicated

It is again advisable to avoid travel to malaria endemic regions with children if avoidable. However, if travel is essential then children should take malarial prophylaxis as they are more at risk of serious complications.

- diethyltoluamide (DEET) 20-50% can be used in children over 2 months of age
- doxycycline is only licensed in the UK for children over the age of 12 years

Which one of the following statements regarding toxoplasmosis is true?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. It is a type of flagellate   |
| <input type="radio"/> | B. Congenital toxoplasmosis results in optic nerve atrophy                            |
| <input type="radio"/> | C. Ceftriaxone should be used initially in patients with HIV-associated toxoplasmosis |
| <input type="radio"/> | D. The cat is the only known animal reservoir   |
| <input type="radio"/> | E. infection is usually self-limiting   |

Next question

## Toxoplasmosis

*Toxoplasma gondii* is a protozoa which infects the body via the GI tract, lung or broken skin. Its oocysts release trophozoites which migrate widely around the body including to the eye, brain and muscle. The usual animal reservoir is the cat, although other animals such as rats carry the disease.

Most infections are asymptomatic. Symptomatic patients usually have a self-limiting infection, often having clinical features resembling infectious mononucleosis (fever, malaise, lymphadenopathy). Other less common manifestations include meningoencephalitis and myocarditis.

### Investigation

- antibody test
- Sabin-Feldman dye test

Treatment is usually reserved for those with severe infections or patients who are immunosuppressed

- pyrimethamine plus sulphadiazine for at least 6 weeks

Congenital toxoplasmosis is due to transplacental spread from the mother. It causes a variety of effects to the unborn child including microcephaly, hydrocephalus, cerebral calcification and chorioretinitis.

A phlebotomist gives herself a needlestick injury whilst taking blood from a patient who is known to be hepatitis B positive. The phlebotomist has just started her job and is in the process of being immunised for hepatitis B but has only had one dose to date. What is the most appropriate action to minimise her risk of contracting hepatitis B from the needle?

<input type="radio"/>	A. No action needed, complete hepatitis B vaccination course as normal
<input type="radio"/>	B. Give oral ribavirin for 4 weeks
<input type="radio"/>	C. Give an accelerated course of the hepatitis B vaccine + hepatitis B immune globulin
<input type="radio"/>	D. Give hepatitis B immune globulin + oral ribavirin for 4 weeks
<input type="radio"/>	E. Give hepatitis B immune globulin

[Next question](#)

## Post-exposure prophylaxis

### Hepatitis A

- Human Normal Immunoglobulin (HNIG) or hepatitis A vaccine may be used depending on the clinical situation

### Hepatitis B

- HBsAg positive source: if the person exposed is a known responder to HBV vaccine then a booster dose should be given. If they are in the process of being vaccinated or are a non-responder they need to have hepatitis B immune globulin (HBIG) and the vaccine
- unknown source: for known responders the green book advises considering a booster dose of HBV vaccine. For known non-responders HBIG + vaccine should be given whilst those in the process of being vaccinated should have an accelerated course of HBV vaccine

### Hepatitis C

- monthly PCR - if seroconversion then interferon +/- ribavirin

### HIV

- a combination of oral antiretrovirals (e.g. Tenofovir, emtricitabine, lopinavir and ritonavir) as soon as possible (i.e. Within 1-2 hours, but may be started up to 72 hours following exposure) for 4 weeks
- serological testing at 12 weeks following completion of post-exposure prophylaxis
- reduces risk of transmission by 80%

Varicella zoster

- VZIG for IgG negative pregnant women/immunosuppressed

**Estimates of transmission risk for single needlestick injury**

Hepatitis B	20-30%
Hepatitis C	0.5-2%
HIV	0.3%



What is the first line antibiotic in the treatment of *Shigella* dysentery?

<input type="radio"/>	A. Flucloxacillin
<input type="radio"/>	B. Vancomycin
<input type="radio"/>	C. Ciprofloxacin
<input type="radio"/>	D. Metronidazole
<input type="radio"/>	E. Ampicillin

Next question

## Shigella

### Overview

- causes bloody diarrhoea, abdo pain
- severity depends on type: *S sonnei* (e.g. from UK) may be mild, *S flexneri* or *S dysenteriae* from abroad may cause severe disease
- treat with ciprofloxacin

Which one of the following conditions is not associated with prior Epstein-Barr virus infection?

<input type="radio"/>	A. Hodgkin's lymphoma
<input type="radio"/>	B. Adult T-cell leukaemia
<input type="radio"/>	C. Burkitt's lymphoma
<input type="radio"/>	D. Nasopharyngeal carcinoma
<input type="radio"/>	E. Hairy leukoplakia

Next question

EBV: associated malignancies:

- Burkitt's lymphoma
- Hodgkin's lymphoma
- nasopharyngeal carcinoma

Adult T-cell leukaemia is associated with HTLV-1 infection

### Epstein-Barr virus: associated conditions

Malignancies associated with EBV infection

- Burkitt's lymphoma\*
- Hodgkin's lymphoma
- nasopharyngeal carcinoma
- HIV-associated central nervous system lymphomas

The non-malignant condition hairy leukoplakia is also associated with EBV infection.

\*EBV is currently thought to be associated with both African and sporadic Burkitt's

A 38-year-old homeless man is diagnosed as having pulmonary tuberculosis. It is decided that directly observed therapy should be used. How often will he need to take anti-tuberculosis medications?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Once a week        |
| <input type="radio"/> | B. Twice a week       |
| <input type="radio"/> | C. Three times a week |
| <input type="radio"/> | D. Five times a week  |
| <input type="radio"/> | E. Once every day     |

[Next question](#)

### Tuberculosis: drug therapy

The standard therapy for treating **active tuberculosis** is:

Initial phase - first 2 months (RIPE)

- Rifampicin
- Isoniazid
- Pyrazinamide
- Ethambutol (the 2006 NICE guidelines now recommend giving a 'fourth drug' such as ethambutol routinely - previously this was only added if drug-resistant tuberculosis was suspected)

Continuation phase - next 4 months

- Rifampicin
- Isoniazid

The treatment for **latent tuberculosis** is isoniazid alone for 6 months

Patients with **meningeal tuberculosis** are treated for a prolonged period (at least 12 months) with the addition of steroids

**Directly observed therapy** with a three times a week dosing regimen may be indicated in certain groups, including:

- homeless people with active tuberculosis
- patients who are likely to have poor concordance
- all prisoners with active or latent tuberculosis

A 44-year-old man who is known to have HIV is admitted to the Emergency Department following a seizure. He has been taking antiretroviral therapy for the past two years. A CT scan (without contrast) shows a solitary lesion in the basal ganglia. What is the most effective method to help differentiate between lymphoma and toxoplasmosis?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. MR spectroscopy       |
| <input type="radio"/> | B. CT with contrast      |
| <input type="radio"/> | C. Thallium SPECT        |
| <input type="radio"/> | D. Peripheral blood film |
| <input type="radio"/> | E. Lumbar puncture       |

[Next question](#)

Differentiating between toxoplasmosis and lymphoma is an important aspect of managing neurocomplications relating to HIV. Given the more limited availability of SPECT compared to CT many patients are treated empirically on the basis of scoring systems, for example there is a 90% likelihood of toxoplasmosis if all of the following criteria are met:

- toxoplasmosis IgG in the serum
- CD4 < 100 and not receiving prophylaxis for toxoplasmosis
- multiple ring enhancing lesions on CT or MRI

## HIV: neurocomplications

### Generalised neurological disease

#### Encephalitis

- may be due to CMV or HIV itself
- HSV encephalitis but is relatively rare in the context of HIV
- CT: oedematous brain

#### *Cryptococcus*

- most common fungal infection of CNS
- headache, fever, malaise, nausea/vomiting, seizures, focal neurological deficit
- CSF: high opening pressure, India ink test positive
- CT: meningeal enhancement, cerebral oedema
- meningitis is typical presentation but may occasionally cause a space occupying lesion

## Progressive multifocal leukoencephalopathy (PML)

- widespread demyelination
- due to infection of oligodendrocytes by human papovirus (JC virus)
- symptoms, subacute onset : behavioural changes, speech, motor, visual impairment
- CT: single or multiple lesions, no mass effect, don't usually enhance. MRI is better - high-signal demyelinating white matter lesions are seen

## AIDS dementia complex

- caused by HIV virus itself
- symptoms: behavioural changes, motor impairment
- CT: cortical and subcortical atrophy

## Focal neurological lesions

### Toxoplasmosis

- accounts for around 50% of cerebral lesions in patients with HIV
- constitutional symptoms, headache, confusion, drowsiness
- CT: usually single or multiple ring enhancing lesions, mass effect may be seen
- management: sulfadiazine and pyrimethamine

### Primary CNS lymphoma

- accounts for around 30% of cerebral lesions
- associated with the Epstein-Barr virus
- CT: single or multiple ring enhancing lesions

Differentiating between toxoplasmosis and lymphoma is a common clinical scenario in HIV patients. It is clearly important given the vastly different treatment strategies. The table below gives some general differences. Please see the Radiopaedia link for more details.

Toxoplasmosis	Lymphoma
Multiple lesions	Single lesion
Rng or nodular enhancement	Solid enhancement
Thallium SPECT negative	Thallium SPECT positive

### Tuberculosis

- much less common than toxoplasmosis or primary CNS lymphoma
- CT: single enhancing lesion

A 23-year-old student returns from India and develops a febrile illness. Following investigation he is diagnosed as having *Plasmodium vivax* malaria. What is the most appropriate treatment?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Chloroquine             |
| <input type="radio"/> | B. Atovaquone-proguanil    |
| <input type="radio"/> | C. Quinine                 |
| <input type="radio"/> | D. Doxycycline             |
| <input type="radio"/> | E. Artemether-lumefantrine |

[Next question](#)

Non-falciparum malarias are almost always chloroquine sensitive

### Malaria: non-falciparum

The most common cause of non-falciparum malaria is *Plasmodium vivax*, with *Plasmodium ovale* and *Plasmodium malariae* accounting for the other cases. *Plasmodium vivax* is often found in Central America and the Indian Subcontinent whilst *Plasmodium ovale* typically comes from Africa

Benign malarias have a hypnozoite stage and may therefore relapse following treatment

#### Treatment

- non-falciparum malarias are almost always chloroquine sensitive
- primaquine should be used following acute treatment with chloroquine to destroy liver hypnozoites and prevent relapse

A nurse undergoes primary immunisation against hepatitis B. Levels of which one of the following should be checked four months later to ensure an adequate response to immunisation?

<input type="radio"/>	A. Anti-HBs
<input type="radio"/>	B. Anti-HBc
<input type="radio"/>	C. Hepatitis B viral load
<input type="radio"/>	D. HbeAg
<input type="radio"/>	E. HBsAg

[Next question](#)

It is preferable to achieve anti-HBs levels above 100 mIU/ml, although levels of 10 mIU/ml or more are generally accepted as enough to protect against infection

### Hepatitis B serology

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months. IgG anti-HBc persists
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

### Example results

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

**Question 93 of 167**

Next

A 45-year-old female presents to the Emergency Department three days after returning from Thailand complaining of severe muscle ache, fever and headache. On examination she has a widespread maculopapular rash. Results show:

Malaria film: negative	
Hb	16.2 *10 <sup>9</sup> g/dl
Plt	96 *10 <sup>9</sup> /l
WBC	2.4 *10 <sup>9</sup> /l
ALT	146 iu/l

What is the most likely diagnosis?

<input type="radio"/>	A. Hepatitis A
<input type="radio"/>	B. Japanese encephalitis
<input type="radio"/>	C. Rheumatic fever
<input type="radio"/>	D. Malaria
<input type="radio"/>	E. Dengue fever

The low platelet count and raised transaminase level is typical of dengue fever

**Dengue fever**

Dengue fever is a type of viral haemorrhagic fever (also yellow fever, Lassa fever, Ebola)

**Basics**

- transmitted by the Aedes aegyti mosquito
- incubation period of 7 days
- a form of disseminated intravascular coagulation (DIC) known as dengue haemorrhagic fever (DHF) may develop. Around 20-30% of these patients go on to develop dengue shock syndrome (DSS)

**Features**

- causes headache (often retro-orbital)
- fever
- myalgia
- pleuritic pain
- facial flushing (dengue)
- maculopapular rash

Treatment is entirely symptomatic e.g. fluid resuscitation, blood transfusion etc



**Question 94 of 167**

Next

A 65-year-old man with a history of type 2 diabetes mellitus and peripheral arterial disease is investigated for fatigue and pyrexia of unknown origin. He recently had an amputation of a toe on his left foot. A diagnosis of osteomyelitis is suspected in the left foot. What is the most appropriate investigation?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. MRI                                      |
| <input type="radio"/> | B. Plain x-ray                              |
| <input type="radio"/> | C. Positron emission tomographic (PET) scan |
| <input type="radio"/> | D. Bone biopsy                              |
| <input type="radio"/> | E. CT scan                                  |

Next question

Osteomyelitis: MRI is the imaging modality of choice

**Osteomyelitis**

Osteomyelitis describes an infection of the bone.

*Staph. aureus* is the most common cause except in patients with sickle-cell anaemia where *Salmonella* species predominate.

**Predisposing conditions**

- diabetes mellitus
- sickle cell anaemia
- intravenous drug user
- immunosuppression due to either medication or HIV
- alcohol excess

**Investigations**

- MRI is the imaging modality of choice, with a sensitivity of 90-100%

**Management**

- flucloxacillin for 6 weeks
- clindamycin if penicillin-allergic

What is the mechanism of action of the antiviral agent amantadine?

<input type="radio"/>	A. Inhibits DNA polymerase
<input type="radio"/>	B. Protease inhibitor
<input type="radio"/>	C. Nucleoside analogue reverse transcriptase inhibitor
<input type="radio"/>	D. Inhibits uncoating of virus in the cell
<input type="radio"/>	E. Interferes with the capping of viral mRNA

Next question

## Antiviral agents

### Aciclovir

- aciclovir is phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase

### Ribavirin

- effective against a range of DNA and RNA viruses
- interferes with the capping of viral mRNA

### Interferons

- inhibit synthesis of mRNA, translation of viral proteins, viral assembly and release

### Amantadine

- used to treat influenza
- inhibits uncoating of virus in cell

## Anti-retroviral agent used in HIV

### Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine

### Protease inhibitors (PI)

- inhibits a protease needed to make the virus able to survive outside the cell
- examples: indinavir, nelfinavir, ritonavir, saquinavir

#### Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz

A 28-year-old man who has recently emigrated from Nigeria presents with a penile ulcer. It initially started as a papule which later progressed to become a painful ulcer with an undermined ragged edge. Examination of the testes was unremarkable but tender inguinal lymphadenopathy was noted. What is the most likely diagnosis?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Chancroid                |
| <input type="radio"/> | B. Lymphogranuloma venereum |
| <input type="radio"/> | C. Syphilis                 |
| <input type="radio"/> | D. Herpes simplex infection |
| <input type="radio"/> | E. Granuloma inguinale      |

Next question

#### Genital ulcers

- painful: herpes much more common than chancroid
- painless: syphilis more common than lymphogranuloma venereum + granuloma inguinale

A diagnosis of chancroid is more likely than lymphogranuloma venereum as the ulcer is painful. Whilst herpes simplex is obviously more common the description of the ulcer is very characteristic of chancroid. Painful inguinal lymphadenopathy is present in around 50% of patients.

#### STI: ulcers

Genital herpes is most often caused by the herpes simplex virus (HSV) type 2 (cold sores are usually due to HSV type 1). Primary attacks are often severe and associated with fever whilst subsequent attacks are generally less severe and localised to one site

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*. Infection is characterised by primary, secondary and tertiary stages. A painless ulcer (chancre) is seen in the primary stage. The incubation period= 9-90 days

Chancroid is a tropical disease caused by *Haemophilus ducreyi*. It causes painful genital ulcers associated with inguinal lymph node enlargement

Lymphogranuloma venereum is caused by *Chlamydia trachomatis*. Typically infection comprises of three stages

- stage 1: small painless pustule which later forms an ulcer
- stage 2: painful inguinal lymphadenopathy
- stage 3: proctocolitis

## Other causes of genital ulcers

- Behcet's disease
- carcinoma
- granuloma inguinale: *Klebsiella granulomatis*\*

\*previously called *Calymmatobacterium granulomatis*

A 24-year-old man presents with a three day history of painful ulcers on the shaft of his penis and dysuria. He has had no similar previous episodes. A clinical diagnosis of primary genital herpes is made. What is the most appropriate management?

<input type="radio"/>	A. Topical famciclovir
<input type="radio"/>	B. No treatment is indicated
<input type="radio"/>	C. Topical podophyllotoxin
<input type="radio"/>	D. Topical valaciclovir
<input type="radio"/>	E. Oral aciclovir

[Next question](#)

Oral antiviral therapy is indicated for primary genital herpes infections, even if the presentation is delayed for up to 5 days

### Herpes simplex virus

There are two strains of the herpes simplex virus (HSV) in humans: HSV-1 and HSV-2. Whilst it was previously thought HSV-1 accounted for oral lesions (cold sores) and HSV-2 for genital herpes it is now known there is considerable overlap

#### Features

- primary infection: may present with a severe gingivostomatitis
- cold sores
- painful genital ulceration

#### Management

- gingivostomatitis: oral aciclovir, chlorhexidine mouthwash
- cold sores: topical aciclovir although the evidence base for this is modest
- genital herpes: oral aciclovir. Some patients with frequent exacerbations may benefit from longer term aciclovir

Which one of the following tests is most likely to remain positive in a patient with syphilis despite treatment?

<input type="radio"/>	A. Wassermann reaction
<input type="radio"/>	B. Rapid plasma reagin (RPR)
<input type="radio"/>	C. Venereal disease research laboratory (VDRL)
<input type="radio"/>	D. Blood culture
<input type="radio"/>	E. <i>Treponema pallidum</i> haemagglutination test (TPHA)

Next question

### Syphilis: investigation

*Treponema pallidum* is a very sensitive organism and cannot be grown on artificial media. The diagnosis is therefore usually based on clinical features, serology and microscopic examination of infected tissue

Serological tests can be divided into

- cardiolipin tests (not treponeme specific)
- treponemal specific antibody tests

Cardiolipin tests

- syphilis infection leads to the production of non-specific antibodies that react to cardiolipin
- examples include VDRL (Venereal Disease Research Laboratory) & RPR (rapid plasma reagin)
- insensitive in late syphilis
- becomes negative after treatment

Treponemal specific antibody tests

- example: TPHA (*Treponema pallidum* HaemAgglutination test)
- remains positive after treatment

Causes of false positive cardiolipin tests

- pregnancy
- SLE, anti-phospholipid syndrome
- TB
- leprosy
- malaria
- HIV

### Question 99 of 167

Which of the following antibiotics is predominately bactericidal?

<input type="radio"/>	A. Trimethoprim
<input type="radio"/>	B. Erythromycin
<input type="radio"/>	C. Ciprofloxacin
<input type="radio"/>	D. Chloramphenicol
<input type="radio"/>	E. Minocycline

[Next question](#)

### Antibiotics: bactericidal vs. bacteriostatic

#### Bactericidal antibiotics

- penicillins
- cephalosporins
- aminoglycosides
- nitrofurantoin
- metronidazole
- quinolones
- rifampicin
- isoniazid

#### Bacteriostatic antibiotics

- chloramphenicol
- macrolides
- tetracyclines
- sulphonamides
- trimethoprim



A health care assistant sustains a needlestick injury whilst taking blood from a patient who is known to be HIV positive. Following thorough washing of the wound what is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. HIV test of health care worker in 3 months to determine treatment   |
| <input type="radio"/> | B. Immediate p24 HIV test of health care worker to determine treatment |
| <input type="radio"/> | C. Oral antiretroviral therapy for 4 weeks                             |
| <input type="radio"/> | D. Oral antiretroviral therapy for 3 months                            |
| <input type="radio"/> | E. Intravenous zidovudine  |

[Next question](#)

Post-exposure prophylaxis for HIV: oral antiretroviral therapy for 4 weeks

## Post-exposure prophylaxis

### Hepatitis A

- Human Normal Immunoglobulin (HNIG) or hepatitis A vaccine may be used depending on the clinical situation

### Hepatitis B

- HBsAg positive source: if the person exposed is a known responder to HBV vaccine then a booster dose should be given. If they are in the process of being vaccinated or are a non-responder they need to have hepatitis B immune globulin (HBIG) and the vaccine
- unknown source: for known responders the green book advises considering a booster dose of HBV vaccine. For known non-responders HBIG + vaccine should be given whilst those in the process of being vaccinated should have an accelerated course of HBV vaccine

### Hepatitis C

- monthly PCR - if seroconversion then interferon +/- ribavirin

### HIV

- a combination of oral antiretrovirals (e.g. Tenofovir, emtricitabine, lopinavir and ritonavir) as soon as possible (i.e. Within 1-2 hours, but may be started up to 72 hours following exposure) for 4 weeks
- serological testing at 12 weeks following completion of post-exposure prophylaxis

- reduces risk of transmission by 80%

Varicella zoster

- VZIG for IgG negative pregnant women/immunosuppressed

#### **Estimates of transmission risk for single needlestick injury**

Hepatitis B	20-30%
Hepatitis C	0.5-2%
HIV	0.3%

Which one of the following is a Gram negative coccus?

<input type="radio"/>	A. <i>Haemophilus influenzae</i>
<input type="radio"/>	B. <i>Moraxella catarrhalis</i>
<input type="radio"/>	C. <i>Enterococcus faecalis</i>
<input type="radio"/>	D. <i>Listeria monocytogenes</i>
<input type="radio"/>	E. <i>Campylobacter jejuni</i>

Next question

### Classification of bacteria

Remember:

- Gram positive cocci = staphylococci + streptococci (including enterococci)
- Gram negative cocci = *Neisseria meningitidis* + *Neisseria gonorrhoeae*, also *Moraxella*

Therefore, only a small list of Gram positive rods (bacilli) need to be memorised to categorise all bacteria - mnemonic = ABCD L

- *Actinomyces*
- *Bacillus anthracis* (anthrax)
- *Clostridium*
- Diphtheria: *Corynebacterium diphtheriae*
- *Listeria monocytogenes*

Remaining organisms are Gram negative rods

A man presents with severe vomiting. He reports not being able to keep fluids down for the past 12 hours. You suspect a diagnosis of gastroenteritis and on discussing possible causes he mentions reheating curry with rice the night before. What is the most likely causative organism?

- ☐ A. *Escherichia coli*
- ☐ B. *Campylobacter*
- ☐ C. *Salmonella*
- ☐ D. *Shigella*
- ☐ E. *Bacillus cereus*

Next question

*Bacillus cereus* infection most commonly results from reheated rice.

### Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

### Stereotypical histories

<b><i>Escherichia coli</i></b>	Common amongst travellers Watery stools Abdominal cramps and nausea
<b>Giardiasis</b>	Prolonged, non-bloody diarrhoea
<b>Cholera</b>	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
<b><i>Shigella</i></b>	Bloody diarrhoea Vomiting and abdominal pain
<b><i>Staphylococcus aureus</i></b>	Severe vomiting Short incubation period
<b><i>Campylobacter</i></b>	A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody  Complications include Guillain-Barre syndrome
<b><i>Bacillus cereus</i></b>	Two types of illness are seen <ul style="list-style-type: none"> <li>vomiting within 6 hours, stereotypically due to rice</li> </ul>

	<ul style="list-style-type: none"> <li>• diarrhoeal illness occurring after 6 hours</li> </ul>
<b>Amoebiasis</b>	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

#### Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus*\*
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

\*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

A patient with HIV is reviewed. Which one of the following is an example of a nucleoside analogue reverse transcriptase inhibitors?

<input type="radio"/>	A. Zidovudine
<input type="radio"/>	B. Indinavir
<input type="radio"/>	C. Ritonavir
<input type="radio"/>	D. Ribavirin
<input type="radio"/>	E. Efavirenz

[Next question](#)

HIV drugs, rule of thumb:

- NRTIs end in 'ine'
- Pis: end in 'vir'
- NNRTIs: nevirapine, efavirenz

Zidovudine (AZT) was one of the first HIV drugs and remains important today.

### HIV: anti-retrovirals

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

Protease inhibitors (PI)

- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system

A 17-year-old girl presents with a sore throat. On examination she has inflamed tonsils covered in white patches. Tender cervical lymphadenopathy and a low grade pyrexia are also present. Which one of the following organisms is most likely to be responsible?

<input type="radio"/>	A. <i>Streptococcus viridans</i>
<input type="radio"/>	B. <i>Streptococcus agalactiae</i>
<input type="radio"/>	C. <i>Streptococcus pneumoniae</i>
<input type="radio"/>	D. <i>Staphylococcus aureus</i>
<input type="radio"/>	E. <i>Streptococcus pyogenes</i>

[Next question](#)

## Streptococci

Streptococci are gram-positive cocci. They may be divided into alpha and beta haemolytic types

### Alpha haemolytic streptococci (partial haemolysis)

The most important alpha haemolytic *Streptococcus* is *Streptococcus pneumoniae* (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is *Streptococcus viridans*

### Beta haemolytic streptococci (complete haemolysis)

These can be subdivided into groups A-H. Only groups A, B & D are important in humans.

#### Group A

- most important organism is *Streptococcus pyogenes*
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

#### Group B

- *Streptococcus agalactiae* may lead to neonatal meningitis and septicaemia

#### Group D

- *Enterococcus*



Which of the following anti-retroviral drugs is most characteristically associated with pancreatitis?

- |                       |                      |
|-----------------------|----------------------|
| <input type="radio"/> | A. Zidovudine        |
| <input type="radio"/> | <b>B. Didanosine</b> |
| <input type="radio"/> | C. Indinavir         |
| <input type="radio"/> | D. Ritonavir         |
| <input type="radio"/> | E. Nevirapine        |

Next question

Ritonavir may cause acute pancreatitis but this is not as common as with didanosine therapy

#### **HIV: biliary and pancreatic disease**

The most common cause of biliary disease in patients with HIV is sclerosing cholangitis due to infections such as CMV, Cryptosporidium and Microsporidia

Pancreatitis in the context of HIV infection may be secondary to anti-retroviral treatment (especially didanosine) or by opportunistic infections e.g. CMV

A 19-year-old man presents asking for advice. His girlfriend has recently been diagnosed with meningococcal meningitis. He is worried he may have 'caught it'. What is the recommended antibiotic prophylaxis for close contacts such as this man?

<input type="radio"/>	A. Oral co-amoxiclav
<input type="radio"/>	B. Oral phenoxymethylpenicillin
<input type="radio"/>	C. Oral rifampicin
<input type="radio"/>	D. Oral erythromycin
<input type="radio"/>	E. Intramuscular cefotaxime

The BNF recommends a twice a day dose of rifampicin for two days, based on the patients weight.

### Meningitis: management

Investigations suggested by NICE

- full blood count
- CRP
- coagulation screen
- blood culture
- whole-blood PCR
- blood glucose
- blood gas

Lumbar puncture if no signs of raised intracranial pressure

### Management

All patients should be transferred to hospital urgently. If patients are in a pre-hospital setting (for example a GP surgery) and meningococcal disease is suspected then intramuscular benzylpenicillin may be given, as long as this doesn't delay transit to hospital.

BNF recommendations on antibiotics

Initial empirical therapy aged 3 months - 50 years	Intravenous cefotaxime
Initial empirical therapy aged > 50 years	Intravenous cefotaxime + amoxicillin
Meningococcal meningitis	Intravenous benzylpenicillin or cefotaxime
Pneumococcal meningitis	Intravenous cefotaxime
Meningitis caused by <i>Haemophilus influenzae</i>	Intravenous cefotaxime
Meningitis caused by <i>Listeria</i>	Intravenous amoxicillin + gentamicin

If the patient has a history of immediate hypersensitivity reaction to penicillin or to cephalosporins the BNF recommends using chloramphenicol.

#### Management of contacts

- prophylaxis needs to be offered to household and close contacts of patients affected with meningococcal meningitis
- oral rifampicin or ciprofloxacin may be used
- the risk is highest in the first 7 days but persists for at least 4 weeks
- meningococcal vaccination should be offered when serotype results are available, for close contacts who have not previously been vaccinated

A baby is born to a mother who is known to have chronic hepatitis B. The mothers latest results are as follows:

HBsAg	Positive
HBeAg	Positive

What is the most appropriate strategy for reducing the vertical transmission rate?

- ☐ A. Give the newborn hepatitis B vaccine + hepatitis B immunoglobulin
- ☐ B. Give the newborn hepatitis B vaccine
- ☐ C. Give the newborn hepatitis B immunoglobulin
- ☐ D. Give the mother intravenous zidovudine during labour
- ☐ E. Give the mother hepatitis B immunoglobulin shortly before birth + the newborn hepatitis B vaccine

Next question

HBeAg is a marker of infectivity. If the mother was anti-HBe positive only the vaccine would need to be administered. Please see the link for more details.

## Hepatitis B and pregnancy

### Basics

- all pregnant women are offered screening for hepatitis B
- babies born to mothers who are chronically infected with hepatitis B or to mothers who've had acute hepatitis B during pregnancy should receive a complete course of vaccination + hepatitis B immunoglobulin
- studies are currently evaluating the role of oral antiviral treatment (e.g. Lamivudine) in the latter part of pregnancy
- there is little evidence to suggest caesarean section reduces vertical transmission rates
- hepatitis B cannot be transmitted via breastfeeding (in contrast to HIV)

Which of the following infections usually has the longest incubation period?

<input type="radio"/>	A. Typhoid
<input type="radio"/>	B. Diphtheria
<input type="radio"/>	C. Dengue fever
<input type="radio"/>	D. Measles
<input type="radio"/>	E. Chickenpox

[Next question](#)

### Incubation periods

Questions may either ask directly about incubation periods or they may be used to provide a clue in a differential diagnosis

Less than 1 week

- meningococcus
- diphtheria
- influenza
- scarlet fever

1 - 2 weeks

- malaria
- dengue fever
- typhoid
- measles

2 - 3 weeks

- mumps
- rubella
- chickenpox

Longer than 3 weeks

- infectious mononucleosis
- cytomegalovirus
- viral hepatitis
- HIV

What is the mechanism of action of rifampicin?

<input type="radio"/>	A. Inhibits DNA synthesis
<input type="radio"/>	B. Interferes with cell wall formation
<input type="radio"/>	C. Inhibits RNA synthesis
<input type="radio"/>	D. Causes misreading of mRNA
<input type="radio"/>	E. Inhibits protein synthesis

Next question

### Antibiotics: mechanisms of action

The lists below summarise the site of action of the commonly used antibiotics

Inhibit cell wall formation

- penicillins
- cephalosporins

Inhibit protein synthesis

- aminoglycosides (cause misreading of mRNA)
- chloramphenicol
- macrolides (e.g. erythromycin)
- tetracyclines
- fusidic acid

Inhibit DNA synthesis

- quinolones (e.g. ciprofloxacin)
- metronidazole
- sulphonamides
- trimethoprim

Inhibit RNA synthesis

- rifampicin

A 31-year-old female presents to the genitourinary medicine clinic due to four fleshy, protuberant lesions on her vulva which are slightly pigmented. She has recently started a relationship with a new partner. What is the most appropriate initial management?

<input type="radio"/>	A. Oral aciclovir
<input type="radio"/>	B. Topical podophyllum
<input type="radio"/>	C. Topical salicylic acid
<input type="radio"/>	D. Topical aciclovir
<input type="radio"/>	E. Electrocautery

[Next question](#)

#### Genital wart treatment

- multiple, non-keratinised warts: topical podophyllum
- solitary, keratinised warts: cryotherapy

Cryotherapy is also acceptable as an initial treatment for genital warts

#### Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

#### Features

- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

#### Management

- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment and recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

A 31-year-old man from Russia who is known to be HIV positive presents with purple plaques on his skin. Which of the following viruses is thought to be the cause of Kaposi's sarcoma?

<input type="radio"/>	A. HTLV-1
<input type="radio"/>	B. HIV-2
<input type="radio"/>	C. HHV-8
<input type="radio"/>	D. CMV
<input type="radio"/>	E. HPV-8

[Next question](#)

Kaposi's sarcoma - caused by HHV-8 (human herpes virus 8)

### HIV: Kaposi's sarcoma

Kaposi's sarcoma

- caused by HHV-8 (human herpes virus 8)
- presents as purple papules or plaques on the skin or mucosa (e.g. gastrointestinal and respiratory tract)
- skin lesions may later ulcerate
- respiratory involvement may cause massive haemoptysis and pleural effusion
- radiotherapy + resection



Which one of the following is least associated with rabies?

<input type="radio"/>	A. Hydrophobia
<input type="radio"/>	B. Opisthotonus
<input type="radio"/>	C. Pyrexia
<input type="radio"/>	D. Headache
<input type="radio"/>	E. Hypersalivation

Next question

Opisthotonus is associated more with tetanus. It describes a state of a hyperextension and spasticity in which a patient's neck and spinal column enter into an arching position. It is an extrapyramidal effect and is caused by spasm of the axial muscles

## Rabies

### Features

- prodrome: headache, fever, agitation
- hydrophobia: water-provoking muscle spasms
- hypersalivation

There is now considered to be 'no risk' of developing rabies following an animal bite in the UK and the majority of developed countries. Following an animal bite in at risk countries:

- if an individual is already immunised then 2 further doses of vaccine should be given
- if not previously immunised then human rabies immunoglobulin (HRIG) should be given along with a full course of vaccination

**Question 113 of 167**

Next

A 22-year-old woman presents with lethargy, pyrexia and headaches. She is a student and returned from a holiday in Ibiza ten days ago. These symptoms have been present for the past six days and she is wondering whether she may need an antibiotic. She also has a history of menorrhagia and is concerned that she may be anaemic. Clinical examination reveals a temperature of 37.9°C and marked cervical lymphadenopathy. You order a full blood count which is reported as follows:

Hb	12.1 g/dl
Platelets	$189 \times 10^9/l$
WCC	$13.1 \times 10^9/l$
Neutrophils	$5.2 \times 10^9/l$
Lymphocytes	$6.2 \times 10^9/l$
Film	Atypical lymphocytes seen

What is the most likely diagnosis?

- ☐ A. Acute lymphoblastic leukaemia
- ☐ B. Hashimoto's thyroiditis
- ☐ C. Infectious mononucleosis
- ☐ D. HIV seroconversion
- ☐ E. Septicaemia secondary to streptococcal throat infection

Next question

Atypical lymphocytes - ?glandular fever

**Infectious mononucleosis**

Infectious mononucleosis (glandular fever) is caused by the Epstein-Barr virus (also known as human herpesvirus 4, HHV-4). It is most common in adolescents and young adults.

**Features**

- sore throat
- lymphadenopathy
- pyrexia
- malaise, anorexia, headache
- palatal petechiae
- splenomegaly - occurs in around 50% of patients and may rarely predispose to splenic rupture

- hepatitis
- presence of 50% lymphocytes with at least 10% atypical lymphocytes
- haemolytic anaemia
- a maculopapular, pruritic rash develops in around 99% of patients who take ampicillin/amoxicillin whilst they have infectious mononucleosis

Management is supportive and includes:

- rest during the early stages, drink plenty of fluid, avoid alcohol
- simple analgesia for any aches or pains
- consensus guidance in the UK is to avoid playing contact sports for 8 weeks after having glandular fever to reduce the risk of splenic rupture

A 45-year-old man presents with pain and swelling of his left big toe. He has recently started treatment for active tuberculosis. Which one of the following medications is likely to be responsible?

<input type="radio"/>	A. Streptomycin
<input type="radio"/>	B. Rifampicin
<input type="radio"/>	C. Ethambutol
<input type="radio"/>	D. Isoniazid
<input type="radio"/>	E. Pyrazinamide

[Next question](#)

There are case reports of ethambutol-induced gout but it is not listed as a side-effect in the BNF

### **Tuberculosis: drug side-effects**

Common side effects:

Rifampicin

- potent liver enzyme inducer
- hepatitis, orange secretions
- flu-like symptoms

Isoniazid

- peripheral neuropathy: prevent with pyridoxine (Vitamin B6)
- hepatitis, agranulocytosis
- liver enzyme inhibitor

Pyrazinamide

- hyperuricaemia causing gout
- hepatitis

Ethambutol

- optic neuritis: check visual acuity before and during treatment
- dose needs adjusting in patients with renal impairment

A 34-year-old female presents with fever and lower abdominal pain. Over the past five days she has noticed deep dyspareunia and some post-coital bleeding. Her last period began 10 days ago. She is diffusely tender in the suprapubic area and vaginal examination reveals cervical excitation. Endocervical swabs are taken. A diagnosis of pelvic inflammatory disease is suspected. What is the most appropriate management?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Oral doxycycline                 |
| <input type="radio"/> | B. Await endocervical swab results  |
| <input type="radio"/> | C. Oral amoxicillin + ciprofloxacin |
| <input type="radio"/> | D. Oral doxycycline + ciprofloxacin |
| <input type="radio"/> | E. Oral ofloxacin + metronidazole   |

[Next question](#)

Consensus guidelines recommend treatment once a diagnosis of pelvic inflammatory disease is suspected, rather than waiting for the results of swabs

### Pelvic inflammatory disease

Pelvic inflammatory disease (PID) is a term used to describe infection and inflammation of the female pelvic organs including the uterus, fallopian tubes, ovaries and the surrounding peritoneum. It is usually the result of ascending infection from the endocervix

#### Causative organisms

- *Chlamydia trachomatis* - the most common cause
- *Neisseria gonorrhoeae*
- *Mycoplasma genitalium*
- *Mycoplasma hominis*

#### Features

- lower abdominal pain
- fever
- deep dyspareunia
- dysuria and menstrual irregularities may occur
- vaginal or cervical discharge
- cervical excitation

#### Investigation

- screen for *Chlamydia* and *Gonorrhoea*

## Management

- due to the difficulty in making an accurate diagnosis, and the potential complications of untreated PID, consensus guidelines recommend having a low threshold for treatment
- oral ofloxacin + oral metronidazole or intramuscular ceftriaxone + oral doxycycline + oral metronidazole
- RCOG guidelines suggest that in mild cases of PID intrauterine contraceptive devices may be left in

## Complications

- infertility - the risk may be as high as 10-20% after a single episode
- chronic pelvic pain
- ectopic pregnancy

A 30-year-old man comes for review. He lives with a woman who has recently being diagnosed with having tuberculosis. The man was born in the UK, has no past medical history of note and is currently asymptomatic. His records show that he had the BCG vaccination as a child. What is the most appropriate test to check for latent tuberculosis?

- ☐ A. Heaf test
- ☐ B. Mantoux test
- ☐ C. Sputum culture
- ☐ D. Chest x-ray
- ☐ E. Interferon-gamma blood test

Next question

The two main tests used for screening in the UK are the Mantoux (skin) test and the interferon-gamma (blood) test. Whilst the use of the interferon-gamma test is increasing it is still reserved for specific situations, none of which apply in this case. Please see the NICE guidelines for more details.

The Heaf test is no longer used in the UK.

### Tuberculosis: screening

The Mantoux test is the main technique used to screen for latent tuberculosis. In recent years the interferon-gamma blood test has also been introduced. It is used in a number of specific situations such as:

- the Mantoux test is positive or equivocal
- people where a tuberculin test may be falsely negative (see below)

### Mantoux test

- 0.1 ml of 1:1,000 purified protein derivative (PPD) injected intradermally
- result read 2-3 days later

Diameter of induration	Positivity	Interpretation
< 6mm	Negative - no significant hypersensitivity to tuberculin protein	Previously unvaccinated individuals may be given the BCG
6 - 15mm	Positive - hypersensitive to tuberculin protein	Should not be given BCG. May be due to previous TB infection or BCG
> 15mm	Strongly positive - strongly hypersensitive to tuberculin protein	Suggests tuberculosis infection.

False negative tests may be caused by:

- miliary TB
- sarcoidosis
- HIV
- lymphoma
- very young age (e.g. < 6 months)

### **Heaf test**

The Heaf test was previously used in the UK but has been since been discontinued. It involved injection of PPD equivalent to 100,000 units per ml to the skin over the flexor surface of the left forearm. It was then read 3-10 days later.



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Next

A 37-year-old sewer worker presents to the Emergency Department with flu-like symptoms and pyrexia for the past 3 days. Since this morning he has started to develop a headache and signs of meningism are found on examination. Blood tests show:

Sodium	145 mmol/l
Potassium	4.7 mmol/l
Urea	10.3 mmol/l
Creatinine	133 µmol/l

What is the antibiotic treatment of choice?

- ☐ A. Co-trimoxazole
- ☐ B. Ciprofloxacin
- ☐ C. Metronidazole
- ☐ D. Benzylpenicillin
- ☐ E. Erythromycin

Next question

Leptospirosis - give penicillin or doxycycline

This patient has leptospirosis. The treatment of choice is benzylpenicillin. A lumbar puncture should ideally be done first to confirm meningeal involvement.

**Leptospirosis**

Also known as Weil's disease\*, leptospirosis is commonly seen in questions referring to sewage workers, farmers, vets or people who work in abattoir. It is caused by the spirochaete *Leptospira interrogans* (serogroup L icterohaemorrhagiae), classically being spread by contact with infected rat urine. Weil's disease should always be considered in high-risk patients with hepatorenal failure

**Features**

- fever
- flu-like symptoms
- renal failure (seen in 50% of patients)
- jaundice
- subconjunctival haemorrhage
- headache, may herald the onset of meningitis

## Management

- high-dose benzylpenicillin or doxycycline

\*the term Weil's disease is sometimes reserved for the most severe 10% of cases that are associated with jaundice

Which one of the following organisms causes lymphogranuloma venereum?

<input type="radio"/>	A. <i>Haemophilus ducreyi</i>
<input type="radio"/>	B. <i>Klebsiella granulomatis</i>
<input type="radio"/>	C. Herpes simplex virus
<input type="radio"/>	D. <i>Chlamydia</i>
<input type="radio"/>	E. <i>Treponema pallidum</i>

Next question

### STI: ulcers

Genital herpes is most often caused by the herpes simplex virus (HSV) type 2 (cold sores are usually due to HSV type 1). Primary attacks are often severe and associated with fever whilst subsequent attacks are generally less severe and localised to one site

Syphilis is a sexually transmitted infection caused by the spirochaete *Treponema pallidum*. Infection is characterised by primary, secondary and tertiary stages. A painless ulcer (chancre) is seen in the primary stage. The incubation period= 9-90 days

Chancroid is a tropical disease caused by *Haemophilus ducreyi*. It causes painful genital ulcers associated with inguinal lymph node enlargement

Lymphogranuloma venereum is caused by *Chlamydia trachomatis*. Typically infection comprises of three stages

- stage 1: small painless pustule which later forms an ulcer
- stage 2: painful inguinal lymphadenopathy
- stage 3: proctocolitis

Other causes of genital ulcers

- Behcet's disease
- carcinoma
- granuloma inguinale: *Klebsiella granulomatis*\*

\*previously called *Calymmatobacterium granulomatis*

A 74-year-old female presents with headache and neck stiffness to the Emergency Department. Following a lumbar puncture the patient was started on IV ceftriaxone. CSF culture grows *Listeria monocytogenes*. What is the most appropriate treatment?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Add IV amoxicillin                     |
| <input type="radio"/> | B. Change to IV amoxicillin + gentamicin  |
| <input type="radio"/> | C. Add IV ciprofloxacin                   |
| <input type="radio"/> | D. Add IV co-amoxiclav                    |
| <input type="radio"/> | E. Continue IV ceftriaxone as monotherapy |

[Next question](#)

The current BNF suggests treatment with amoxicillin/ampicillin + gentamicin. Treatment should be for at least 10-14 days

### Listeria

*Listeria monocytogenes* is a Gram positive bacillus which has the unusual ability to multiply at low temperatures. It is typically spread via contaminated food, typically unpasteurised dairy products. Infection is particularly dangerous to the unborn child where it can lead to miscarriage

Features - can present in a variety of ways

- diarrhoea, flu-like illness
- pneumonia , meningoencephalitis
- ataxia and seizures

Suspected *Listeria* infection should be investigated by taking blood cultures. CSF may reveal a pleocytosis, with 'tumbling motility' on wet mounts

### Management

- *Listeria* is sensitive to amoxicillin/ampicillin (cephalosporins usually inadequate)
- *Listeria* meningitis should be treated with IV amoxicillin/ampicillin and gentamicin

Which one of the following organisms causes West African sleeping sickness?

<input type="radio"/>	A. <i>Leishmania tropica</i>
<input type="radio"/>	B. <i>Trypanosoma gambiense</i>
<input type="radio"/>	C. <i>Trypanosoma rhodesiense</i>
<input type="radio"/>	D. <i>Leishmania mexicana</i>
<input type="radio"/>	E. <i>Trypanosoma cruzi</i>

### Trypanosomiasis

Two main form of this protozoal disease are recognised - African trypanosomiasis (sleeping sickness) and American trypanosomiasis (Chagas' disease)

Two forms of **African trypanosomiasis**, or **sleeping sickness**, are seen - *Trypanosoma gambiense* in West Africa and *Trypanosoma rhodesiense* in East Africa. Both types are spread by the tsetse fly. *Trypanosoma rhodesiense* tends to follow a more acute course. Clinical features include:

- *Trypanosoma* chancre - tender subcutaneous nodule at site of infection
- enlargement of posterior cervical lymph nodes
- later: central nervous system involvement e.g. meningoencephalitis

#### Management

- early disease: IV pentamidine or suramin
- later disease or central nervous system involvement: IV melarsoprol

**American trypanosomiasis**, or **Chagas' disease**, is caused by the protozoan *Trypanosoma cruzi*. The vast majority of patients (95%) are asymptomatic in the acute phase although a chagoma (an erythematous nodule at site of infection) and periorbital oedema are sometimes seen. Chronic Chagas' disease mainly affects the heart and gastrointestinal tract

- myocarditis may lead to heart failure and arrhythmias
- gastrointestinal features includes megaesophagus and megacolon causing dysphagia and constipation

#### Management

- treatment is most effective in the acute phase using azole or nitroderivatives such as benznidazole or nifurtimox
- chronic disease management involves treating the complications e.g., heart failure

An 18-year-old man is bitten by a frantic dog whilst taking a gap year in Ecuador. He is worried about rabies and phones for advice. He was not immunised against prior to travelling to Ecuador. What is the most appropriate advice after thorough cleansing of the wound?

<input type="radio"/>	A. Give human rabies immunoglobulin + full course of vaccination
<input type="radio"/>	B. Give human rabies immunoglobulin + oral penicillin for the next 2 weeks
<input type="radio"/>	C. Advise low risk but take oral co-amoxiclav for the dog bite
<input type="radio"/>	D. Give human rabies immunoglobulin
<input type="radio"/>	E. Give full course of vaccination

[Next question](#)

Rabies - following possible exposure give immunoglobulin + vaccination

## Rabies

### Features

- prodrome: headache, fever, agitation
- hydrophobia: water-provoking muscle spasms
- hypersalivation

There is now considered to be 'no risk' of developing rabies following an animal bite in the UK and the majority of developed countries. Following an animal bite in at risk countries:

- if an individual is already immunised then 2 further doses of vaccine should be given
- if not previously immunised then human rabies immunoglobulin (HRIG) should be given along with a full course of vaccination

A 12-year-old boy who had a splenectomy following a road traffic accident is reviewed in clinic. He had his full immunisation course as a child and was given a repeat pneumococcal vaccination 5 days following surgery. What is the most appropriate ongoing management?

<input type="radio"/>	A. Booster dose of Hib and MenC vaccine + lifelong penicillin V
<input type="radio"/>	B. Booster dose of Hib and MenC vaccine + penicillin V for 2 years
<input type="radio"/>	C. Lifelong penicillin V
<input type="radio"/>	D. Booster dose of Hib and MenC vaccine + annual influenza vaccination + penicillin V for 2 years
<input type="radio"/>	E. Booster dose of Hib and MenC vaccine + annual influenza vaccination + lifelong penicillin V

[Next question](#)

Debate still exists regarding how long a patient should take penicillin prophylaxis for. The majority of doctors advocate lifelong penicillin. Consensus guidelines agree however that in this case prophylaxis should be continued until the patient is at least 16 years old, so of the available options E is the correct answer

## Splenectomy

Following a splenectomy patients are particularly at risk from pneumococcus, Haemophilus, meningococcus and Capnocytophaga canimorsus\* infections

### Vaccination

- if elective, should be done 2 weeks prior to operation
- Hib, meningitis A & C
- annual influenza vaccination
- pneumococcal vaccine every 5 years

### Antibiotic prophylaxis

- penicillin V: unfortunately clear guidelines do not exist of how long antibiotic prophylaxis should be continued. It is generally accepted though that penicillin should be continued for at least 2 years and at least until the patient is 16 years of age, although the majority of patients are usually put on antibiotic prophylaxis for life

\*usually from dog bites

**Question 123 of 167**

Next

A 27-year-old woman develops fever and lymph node swelling after being scratched by her cat. Which one of the organisms is responsible for cat scratch disease?

<input type="radio"/>	A. <i>Bordetella pertussis</i>
<input type="radio"/>	B. <i>Moraxella catarrhalis</i>
<input type="radio"/>	C. <i>Bartonella henselae</i>
<input type="radio"/>	D. <i>Francisella tularensis</i>
<input type="radio"/>	E. <i>Yersinia enterocolitica</i>

Next question

Cat scratch disease - caused by *Bartonella henselae*

**Cat scratch disease**

Cat scratch disease is generally caused by the Gram negative rod *Bartonella henselae*

**Features**

- fever
- history of a cat scratch
- regional lymphadenopathy
- headache, malaise



A 40-year-old man is admitted to the intensive care unit following a severe episode of acute pancreatitis. On the third day of his admission he becomes pyrexial. A septic screen is ordered including cultures taken from both peripheral blood and the internal jugular line. There is no signs of infection on the chest x-ray or urine sample. The microbiology laboratory phone to report signs of bacterial infection in the sample from the central line. What is the most likely organism to be isolated?

- ☐ A. *Pseudomonas aeruginosa*
- ☐ B. *Escherichia coli*
- ☐ C. *Staphylococcus epidermidis*
- ☐ D. *Streptococcus pneumoniae*
- ☐ E. *Staphylococcus aureus*

[Next question](#)

Most common organism found in central line infections - *Staphylococcus epidermidis*

## Staphylococci

Staphylococci are a common type of bacteria which are often found normal commensal organisms but may also cause invasive disease. Some basic facts include:

- Gram-positive cocci
- facultative anaerobes
- produce catalase

The two main types of Staphylococci you need to know about are *Staphylococcus aureus* and *Staphylococcus epidermidis*.

<i>Staphylococcus aureus</i>	<i>Staphylococcus epidermidis</i>
<ul style="list-style-type: none"> <li>• Coagulase-positive</li> <li>• Causes skin infections, osteomyelitis, toxic shock syndrome</li> </ul>	<ul style="list-style-type: none"> <li>• Coagulase-negative</li> <li>• Cause of central line infections and infective endocarditis</li> </ul>

A 19-year-old man from a travelling community presents to the Emergency Department with breathing difficulties. On examination he has a temperature of 38.2°C and stridor. A diagnosis of acute epiglottitis is suspected. Which one of the following organisms is most likely to be responsible?

<input type="radio"/>	A. Epstein Barr Virus
<input type="radio"/>	B. <i>Streptococcus pneumoniae</i>
<input type="radio"/>	C. <i>Neisseria meningitidis</i>
<input checked="" type="radio"/>	D. <i>Haemophilus influenzae</i>
<input type="radio"/>	E. <i>Staphylococcus aureus</i>

[Next question](#)

Patients from travelling communities may not always receive a full course of immunisation.

Acute epiglottitis is of course much more common in young children

### Acute epiglottitis

Acute epiglottitis is rare but serious infection caused by *Haemophilus influenzae* type B. Prompt recognition and treatment is essential as airway obstruction may develop. Epiglottitis generally occurs in children between the ages of 2 and 6 years. The incidence of epiglottitis has decreased since the introduction of the Hib vaccine

#### Features

- rapid onset
- unwell, toxic child
- stridor
- drooling of saliva

Which of the following types of viral meningitis may be characteristically associated with a low cerebrospinal fluid glucose level?

- ☐ A. Mumps
- ☐ B. Cytomegalovirus
- ☐ C. Measles
- ☐ D. HIV
- ☐ E. Echovirus

Mumps meningitis is associated with a low CSF glucose

Mumps meningitis is associated with a low glucose in up to a third of patients

### Meningitis: CSF analysis

The table below summarises the characteristic cerebrospinal fluid (CSF) findings in meningitis:

	Bacterial	Viral	Tuberculous
<b>Appearance</b>	Cloudy	Clear/cloudy	Fibrin web
<b>Glucose</b>	Low (< 1/2 plasma)	Normal*	Low (< 1/2 plasma)
<b>Protein</b>	High (> 1 g/l)	Normal/raised	High (> 1 g/l)
<b>White cells</b>	10 - 5,000 polymorphs/mm <sup>3</sup>	15 - 1,000 lymphocytes/mm <sup>3</sup>	10 - 1,000 lymphocytes/mm <sup>3</sup>

The Ziehl-Neelsen stain is only 20% sensitive in the detection of tuberculous meningitis and therefore PCR is sometimes used (sensitivity = 75%)

\*mumps is unusual in being associated with a low glucose level in a proportion of cases. A low glucose may also be seen in herpes encephalitis

Serum glucose 4.9 mmol/l

Lumbar puncture reveals:

Opening pressure	14 cmCSF
Appearance	Cloudy
Glucose	1.7 mmol/l
Protein	1.9 g/l
White cells	900 / mm <sup>3</sup> (90% polymorphs)

A 39-year-old man returns from a two week business trip to Kenya. Four weeks after his return he presents complaining of malaise, headaches and night sweats. On examination there is a symmetrical erythematous macular rash over his trunk and limbs associated with cervical and inguinal lymphadenopathy. What is the most likely diagnosis?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Typhoid fever       |
| <input type="radio"/> | B. Tuberculosis        |
| <input type="radio"/> | C. Dengue fever        |
| <input type="radio"/> | D. Schistosomiasis     |
| <input type="radio"/> | E. Acute HIV infection |

[Next question](#)

Man returns from trip abroad with maculopapular rash and flu-like illness - think HIV seroconversion

Stereotypes are alive and well in the MRCP exam. For questions involving businessmen always consider sexually transmitted infections. The HIV prevalence rate in Kenya is currently around 8%.

### HIV: seroconversion

HIV seroconversion is symptomatic in 60-80% of patients and typically presents as a glandular fever type illness. Increased symptomatic severity is associated with poorer long term prognosis. It typically occurs 3-12 weeks after infection

#### Features

- sore throat
- lymphadenopathy
- malaise, myalgia, arthralgia
- diarrhoea
- maculopapular rash
- mouth ulcers
- rarely meningoencephalitis

#### Diagnosis

- antibodies to HIV may not be present
- HIV PCR and p24 antigen tests can confirm diagnosis

A 62-year-old woman who has recently been treated for ascending cholangitis is referred to hospital due to persistent fever and anorexia. An ultrasound scan reveals the presence of a liver abscess. What is the most appropriate antibiotic therapy to accompany drainage of the abscess?

<input type="radio"/>	A. Vancomycin + meropenem
<input type="radio"/>	B. Co-amoxiclav + metronidazole
<input type="radio"/>	C. Amoxicillin + ciprofloxacin + metronidazole
<input type="radio"/>	D. Clindamycin + metronidazole
<input type="radio"/>	E. Metronidazole + vancomycin

[Next question](#)

### Pyogenic liver abscess

#### Management

- drainage (needle aspiration or catheter) should always be performed
- amoxicillin + ciprofloxacin + metronidazole
- if penicillin allergic: ciprofloxacin + clindamycin

A prison GP is bitten by a patient who is known to have hepatitis B. The GP has a documented full history of hepatitis B vaccination and was known to be a responder. What is the most appropriate action to reduce the chance of contracting hepatitis B?

<input type="radio"/>	A. Admit for intravenous interferon
<input type="radio"/>	B. Give hepatitis B immune globulin
<input type="radio"/>	C. Give hepatitis B immune globulin + hepatitis B vaccine booster
<input type="radio"/>	D. Give hepatitis B vaccine booster
<input type="radio"/>	E. Give oral ribavirin for 4 weeks

[Next question](#)

### Post-exposure prophylaxis

#### Hepatitis A

- Human Normal Immunoglobulin (HNIG) or hepatitis A vaccine may be used depending on the clinical situation

#### Hepatitis B

- HBsAg positive source: if the person exposed is a known responder to HBV vaccine then a booster dose should be given. If they are in the process of being vaccinated or are a non-responder they need to have hepatitis B immune globulin (HBIG) and the vaccine
- unknown source: for known responders the green book advises considering a booster dose of HBV vaccine. For known non-responders HBIG + vaccine should be given whilst those in the process of being vaccinated should have an accelerated course of HBV vaccine

#### Hepatitis C

- monthly PCR - if seroconversion then interferon +/- ribavirin

#### HIV

- a combination of oral antiretrovirals (e.g. Tenofovir, emtricitabine, lopinavir and ritonavir) as soon as possible (i.e. Within 1-2 hours, but may be started up to 72 hours following exposure) for 4 weeks
- serological testing at 12 weeks following completion of post-exposure prophylaxis
- reduces risk of transmission by 80%

Varicella zoster

- VZIG for IgG negative pregnant women/immunosuppressed

**Estimates of transmission risk for single needlestick injury**

Hepatitis B	20-30%
Hepatitis C	0.5-2%
HIV	0.3%

A 31-year-old woman who is known to be HIV positive presents following a positive pregnancy test. Her last menstrual period was 6 weeks ago. The last CD4 count was  $420 \times 10^6/l$  and she does not take any antiretroviral therapy. What is the most appropriate management with regards to antiretroviral therapy?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Check CD4 at 12 weeks and initiate antiretroviral therapy if CD4 count is less than $350 \times 10^6/l$ |
| <input type="radio"/> | B. Do not give antiretroviral therapy  |
| <input type="radio"/> | C. Start antiretroviral therapy at 20-32 weeks   |
| <input type="radio"/> | D. Start antiretroviral therapy at 10-12 weeks   |
| <input type="radio"/> | E. Start antiretroviral therapy immediately  |

[Next question](#)

Whilst the RCOG guidelines recommend 28-32 weeks the BHIVA suggest a slightly earlier gestation may be suitable depending on individual circumstances. The most suitable answer is therefore 20-32 weeks.

### HIV and pregnancy

With the increased incidence of HIV infection amongst the heterosexual population there are an increasing number of HIV positive women giving birth in the UK. In London the incidence may be as high as 0.4% of pregnant women. The aim of treating HIV positive women during pregnancy is to minimise harm to both the mother and fetus, and to reduce the chance of vertical transmission.

Factors which reduce vertical transmission (from 25-30% to 2%)

- maternal antiretroviral therapy
- mode of delivery (caesarean section)
- neonatal antiretroviral therapy
- infant feeding (bottle feeding)

### Screening

- NICE guidelines recommend offering HIV screening to all pregnant women

### Antiretroviral therapy

- all pregnant women should be offered antiretroviral therapy regardless of whether they were taking it previously
- if women are not currently taking antiretroviral therapy the RCOG recommend that it is commenced between 28 and 32 weeks of gestation and should be continued intrapartum. BHIVA recommend that antiretroviral therapy may be started at an earlier gestation depending upon the individual situation



## Mode of delivery

- elective caesarean section\*
- a zidovudine infusion should be started four hours before beginning the caesarean section

## Neonatal antiretroviral therapy

- zidovudine is usually administered orally to the neonate for four to six weeks

## Infant feeding

- in the UK all women should be advised not to breast feed

\*the 2008 BHIVA guidelines suggest vaginal delivery may be an option for women on HAART who have an undetectable viral load but whether this will translate into clinical practice remains to be seen

A 60-year-old man with a past medical history of osteoarthritis presents with a swollen, red and hot left knee joint. He is unable to move it due to the pain. On examination he is pyrexial with a temperature of 38.7 C and a blood sample shows a white cell count of  $22.8 \times 10^9/l$ . Following joint aspiration, what is the most appropriate antibiotic therapy?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. IV flucloxacillin + benzylpenicillin          |
| <input type="radio"/> | B. IV gentamicin + benzylpenicillin              |
| <input type="radio"/> | C. IV flucloxacillin                             |
| <input type="radio"/> | D. IV vancomycin + cefotaxime                    |
| <input type="radio"/> | E. IV gentamicin + rifampicin + benzylpenicillin |

Next question

Septic arthritis: IV flucloxacillin

## Septic arthritis

### Overview

- most common organism overall is *Staphylococcus aureus*
- in young adults who are sexually active *Neisseria gonorrhoeae* should also be considered

### Management

- synovial fluid should be obtained before starting treatment
- intravenous antibiotics which cover Gram-positive cocci are indicated. The BNF currently recommends flucloxacillin or clindamycin if penicillin allergic
- antibiotic treatment is normally be given for several weeks (BNF states 6-12 weeks)
- needle aspiration should be used to decompress the joint
- surgical drainage may be needed if frequent needle aspiration is required

A 27-year-old pregnant woman is found to have *Chlamydia*. What is the most appropriate treatment?

- |                       |                                       |
|-----------------------|---------------------------------------|
| <input type="radio"/> | A. No antibiotic therapy is indicated |
| <input type="radio"/> | B. Cefixime                           |
| <input type="radio"/> | C. Erythromycin                       |
| <input type="radio"/> | D. Doxycycline                        |
| <input type="radio"/> | E. Ciprofloxacin                      |

Next question

Erythromycin or amoxicillin is currently recommended for pregnant or breast feeding women. The efficacy of amoxicillin, often assumed to be ineffective against *Chlamydia*, was supported in a recent Cochrane review. A test of cure should be carried out following treatment.

### ***Chlamydia***

*Chlamydia* is the most prevalent sexually transmitted infection in the UK and is caused by *Chlamydia trachomatis*, an obligate intracellular pathogen. Approximately 1 in 10 young women in the UK have *Chlamydia*. The incubation period is around 7-21 days, although it should be remembered a large percentage of cases are asymptomatic

#### Features

- asymptomatic in around 70% of women and 50% of men
- women: cervicitis (discharge, bleeding), dysuria
- men: urethral discharge, dysuria

#### Potential complications

- epididymitis
- pelvic inflammatory disease
- endometritis
- increased incidence of ectopic pregnancies
- infertility
- reactive arthritis
- perihepatitis (Fitz-Hugh-Curtis syndrome)

#### Investigation

- traditional cell culture is no longer widely used
- nuclear acid amplification tests (NAATs) are now rapidly emerging as the investigation of choice

- urine (first void urine sample), vulvovaginal swab or cervical swab may be tested using the NAAT technique

## Screening

- in England the National *Chlamydia* Screening Programme is open to all men and women aged 15-24 years
- the 2009 SIGN guidelines support this approach, suggesting screening all sexually active patients aged 15-24 years
- relies heavily on opportunistic testing

## Management

- doxycycline (7 day course) or azithromycin (single dose). The 2009 SIGN guidelines suggest azithromycin should be used first-line due to potentially poor compliance with a 7 day course of doxycycline
- if pregnant then erythromycin or amoxicillin may be used. The SIGN guidelines suggest considering azithromycin 'following discussion of the balance of benefits and risks with the patient'
- patients diagnosed with *Chlamydia* should be offered a choice of provider for initial partner notification - either trained practice nurses with support from GUM, or referral to GUM
- for men with symptomatic infection all partners from the four weeks prior to the onset of symptoms should be contacted
- for women and asymptomatic men all partners from the last six months or the most recent sexual partner should be contacted
- contacts of confirmed *Chlamydia* cases should be offered treatment prior to the results of their investigations being known (treat then test)

A 43-year-old sheep farmer presents with a lesion on his right hand. It initially started as a small, raised, red papule but has now become larger. On examination a 2cm, flat-topped haemorrhagic lesion is seen. What is the most likely diagnosis?

<input type="radio"/>	A. Orf
<input type="radio"/>	B. Staphylococcal furuncle
<input type="radio"/>	C. Hand, foot and mouth disease
<input type="radio"/>	D. Paronychia
<input type="radio"/>	E. Anthrax

[Next question](#)

## Orf

Orf is generally a condition found in sheep and goats although it can be transmitted to humans. It is caused by the parapox virus.

In animals

- 'scabby' lesions around the mouth and nose

In humans

- generally affects the hands and arms
- initially small, raised, red-blue papules
- later may increase in size to 2-3 cm and become flat-topped and haemorrhagic

A 35-year-old woman is referred to hospital. As part of a liver screen the following results are obtained:

Anti-HBs	Negative
Anti-HBc	Positive
HBs antigen	Positive
IgM anti-HBc	Negative

Anti-HBs = Hepatitis B Surface Antibody; Anti-HBc = Hepatitis B Core Antibody; HBs antigen = Hepatitis B Surface Antigen

What is the patient's hepatitis B status?

- ☐ A. Probable hepatitis D infection
- ☐ B. Acute hepatitis B infection
- ☐ C. Previous immunisation to hepatitis B
- ☐ D. Chronic hepatitis B
- ☐ E. Previous hepatitis B infection, not a carrier

Next question

The negative IgM anti-HBc points to a chronic rather than acute infection.

### Hepatitis B serology

Interpreting hepatitis B serology is a dying art form which still occurs at regular intervals in medical exams. It is important to remember a few key facts:

- surface antigen (HBsAg) is the first marker to appear and causes the production of anti-HBs
- HBsAg normally implies acute disease (present for 1-6 months)
- if HBsAg is present for > 6 months then this implies chronic disease (i.e. Infective)
- Anti-HBs implies immunity (either exposure or immunisation). It is negative in chronic disease
- Anti-HBc implies previous (or current) infection. IgM anti-HBc appears during acute or recent hepatitis B infection and is present for about 6 months. IgG anti-HBc persists
- HbeAg results from breakdown of core antigen from infected liver cells as is therefore a marker of infectivity

### Example results

- previous immunisation: anti-HBs positive, all others negative
- previous hepatitis B (> 6 months ago), not a carrier: anti-HBc positive, HBsAg negative
- previous hepatitis B, now a carrier: anti-HBc positive, HBsAg positive

A 23-year-old man is admitted to the Emergency Department with an evolving purpuric rash, pyrexia and confusion. His GP had given him intramuscular benzylpenicillin in the surgery and dialled 999. Which one of the following investigations is most likely to reveal the diagnosis?

<input type="radio"/>	A. Urinary antigen
<input type="radio"/>	B. Blood PCR for meningococcus
<input type="radio"/>	C. Blood culture
<input type="radio"/>	D. CT head
<input type="radio"/>	E. Lumbar puncture

[Next question](#)

The blood cultures are likely to be negative as antibiotics have already been given. PCR has a sensitivity of over 90%.

### Meningococcal septicaemia: investigations

Meningococcal septicaemia is a frightening condition for patients, parents and doctors. It is associated with a high morbidity and mortality unless treated early - meningococcal disease is the leading infectious cause of death in early childhood. A high index of suspicion is therefore needed. Much of the following is based on the 2010 NICE guidelines (please see link).

Presentation of meningococcal disease:

- 15% - meningitis
- 25% - septicaemia
- 60% - a combination of meningitis and septicaemia

Investigations

- blood cultures
- blood PCR
- lumbar puncture is usually contraindicated
- full blood count and clotting to assess for disseminated intravascular coagulation

A 19-year-old woman is reviewed in the genitourinary medicine clinic. She presented with vaginal discharge and dysuria. Microscopy of an endocervical swab showed a Gram-negative coccus that was later identified as *Neisseria gonorrhoea*. This is her third episode of gonorrhoea in the past two years. What is the most likely complication from repeated infection?

- |                                  |                             |
|----------------------------------|-----------------------------|
| <input type="radio"/>            | A. Lymphogranuloma venereum |
| <input type="radio"/>            | B. Cervical cancer          |
| <input type="radio"/>            | C. Arthropathy              |
| <input checked="" type="radio"/> | D. Infertility              |
| <input type="radio"/>            | E. Uterine abscess          |

[Next question](#)

Infertility secondary to pelvic inflammatory disease (PID) is the most common complication of gonorrhoea. It is the second most common cause of PID after *Chlamydia*. Arthropathy may occur but it is far less common.

Lymphogranuloma venereum is caused by *Chlamydia trachomatis*.

## Gonorrhoea

Gonorrhoea is caused by the Gram negative diplococcus *Neisseria gonorrhoea*. Acute infection can occur on any mucous membrane surface, typically genitourinary but also rectum and pharynx. The incubation period of gonorrhoea is 2-5 days

### Features

- males: urethral discharge, dysuria
- females: cervicitis e.g. leading to vaginal discharge
- rectal and pharyngeal infection is usually asymptomatic

Local complications that may develop include urethral strictures, epididymitis and salpingitis (hence may lead to infertility). Disseminated infection may occur - see below

### Management

- ciprofloxacin 500mg PO used to be the treatment of choice
- however, there is increased resistance to ciprofloxacin and therefore cephalosporins are now used
- options include cefixime 400mg PO (single dose) or ceftriaxone 250mg IM

Disseminated gonococcal infection (DGI) and gonococcal arthritis may also occur, with gonococcal infection being the most common cause of septic arthritis in young adults. The pathophysiology of DGI is not fully understood but is thought to be due to haematogenous spread from mucosal infection (e.g. Asymptomatic genital



infection). Initially there may be a classic triad of symptoms: tenosynovitis, migratory polyarthrititis and dermatitis. Later complications include septic arthritis, endocarditis and perihepatitis (Fitz-Hugh-Curtis syndrome)

Key features of disseminated gonococcal infection

- tenosynovitis
- migratory polyarthrititis
- dermatitis (lesions can be maculopapular or vesicular)

The most appropriate treatment for cutaneous larva migrans is:

<input type="radio"/>	A. Thiabendazole
<input type="radio"/>	B. Sulfadoxine
<input type="radio"/>	C. Pyrimethamine
<input type="radio"/>	D. Metronidazole
<input type="radio"/>	E. Dapsone

Next question

## Nematodes

*Ancylostoma braziliense*

- most common cause of cutaneous larva migrans
- common in Central and Southern America

*Strongyloides stercoralis*

- acquired percutaneously (e.g. walking barefoot)
- causes pruritus and larva currens - this has a similar appearance to cutaneous larva migrans but moves through the skin at a far greater rate
- abdo pain, diarrhoea, pneumonitis
- may cause Gram negative septicaemia due carrying of bacteria into bloodstream
- eosinophilia sometimes seen
- management: thiabendazole, albendazole. Ivermectin also used, particularly in chronic infections

*Toxocara canis*

- commonly acquired by ingesting eggs from soil contaminated by dog faeces
- commonest cause of visceral larva migrans
- other features: eye granulomas, liver/lung involvement

A 19-year-old medical student undergoes primary immunisation against hepatitis B. His post immunisation bloods are reported as follows:

Anti-HBs	< 10 mIU/ml
----------	-------------

What is the most appropriate course of action?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Give one further dose of hepatitis B vaccine  |
| <input type="radio"/> | B. Do a HIV test   |
| <input type="radio"/> | C. Test for current or past hepatitis B + repeat course (i.e. 3 doses) of vaccine                |
| <input type="radio"/> | D. Give two further doses of hepatitis B vaccine   |
| <input type="radio"/> | E. Give a course of hepatitis B immune globulin (HBIG) + one further dose of hepatitis B vaccine |

Next question

## Hepatitis B

Hepatitis B is a double-stranded DNA virus and is spread through exposure to infected blood or body fluids, including vertical transmission from mother to child. The incubation period is 6-20 weeks.

Immunisation against hepatitis B (please see the Greenbook link for more details)

- contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology
- most schedules give 3 doses of the vaccine with a recommendation for a one-off booster 5 years following the initial primary vaccination
- at risk groups who should be vaccinated include: healthcare workers, intravenous drug users, sex workers, close family contacts of an individual with hepatitis B, individuals receiving blood transfusions regularly, chronic kidney disease patients who may soon require renal replacement therapy, prisoners, chronic liver disease patients
- around 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine. Risk factors include age over 40 years, obesity, smoking, alcohol excess and immunosuppression
- testing for anti-HBs is only recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease. In these patients anti-HBs levels should be checked 1-4 months after primary immunisation
- the table below shows how to interpret anti-HBs levels:

Anti-HBs level (mIU/ml)	Response
> 100	Indicates adequate response, no further testing required. Should still receive booster at 5 years
10 - 100	Suboptimal response - one additional vaccine dose should be given. If immunocompetent no further testing is required
< 10	Non-responder. Test for current or past infection. Give further vaccine course (i.e. 3 doses again) with testing following. If still fails to respond then HBIG would be required for protection if exposed to the virus

### Complications of hepatitis B infection

- chronic hepatitis (5-10%)
- fulminant liver failure (1%)
- hepatocellular carcinoma
- glomerulonephritis
- polyarteritis nodosa
- cryoglobulinaemia

### Management of hepatitis B

- pegylated interferon-alpha used to be the only treatment available. It reduces viral replication in up to 30% of chronic carriers. A better response is predicted by being female, < 50 years old, low HBV DNA levels, non-Asian, HIV negative, high degree of inflammation on liver biopsy
- however due to the side-effects of pegylated interferon it is now used less commonly in clinical practice. Oral antiviral medication is increasingly used with an aim to suppress viral replication (not in dissimilar way to treating HIV patients)
- examples include lamivudine, tenofovir and entecavir

Which one of the following is least associated with a false negative tuberculin skin test?

- ☐ A. Lymphoma
- ☐ B. Miliary tuberculosis
- ☐ C. Sarcoidosis
- ☐ D. Chronic kidney disease stage 3
- ☐ E. HIV

Next question

Severe renal failure may cause a false negative test but CKD stage 3 would not.

### Tuberculosis: screening

The Mantoux test is the main technique used to screen for latent tuberculosis. In recent years the interferon-gamma blood test has also been introduced. It is used in a number of specific situations such as:

- the Mantoux test is positive or equivocal
- people where a tuberculin test may be falsely negative (see below)

### Mantoux test

- 0.1 ml of 1:1,000 purified protein derivative (PPD) injected intradermally
- result read 2-3 days later

Diameter of induration	Positivity	Interpretation
< 6mm	Negative - no significant hypersensitivity to tuberculin protein	Previously unvaccinated individuals may be given the BCG
6 - 15mm	Positive - hypersensitive to tuberculin protein	Should not be given BCG. May be due to previous TB infection or BCG
> 15mm	Strongly positive - strongly hypersensitive to tuberculin protein	Suggests tuberculosis infection.

False negative tests may be caused by:

- miliary TB
- sarcoidosis
- HIV
- lymphoma
- very young age (e.g. < 6 months)

## **Heaf test**

The Heaf test was previously used in the UK but has been since been discontinued. It involved injection of PPD equivalent to 100,000 units per ml to the skin over the flexor surface of the left forearm. It was then read 3-10 days later.

A 24-year-old woman presents due to an itchy vulva and pain during sex. She also mentions a green, offensive vaginal discharge for the past 2 weeks. What is the most likely diagnosis?

<input type="radio"/>	A. <i>Candida</i>
<input type="radio"/>	B. Bacterial vaginosis
<input type="radio"/>	C. Gonorrhoea
<input type="radio"/>	D. <i>Trichomonas vaginalis</i>
<input type="radio"/>	E. <i>Chlamydia</i>

[Next question](#)

## Vaginal discharge

Vaginal discharge is a common presenting symptom and is not always pathological

Common causes

- physiological
- *Candida*
- *Trichomonas vaginalis*
- bacterial vaginosis

Less common causes

- whilst cervical infections such as *Chlamydia* and Gonorrhoea can cause a vaginal discharge this is rarely the presenting symptoms
- ectropion
- foreign body
- cervical cancer

Key features of the common causes are listed below

Condition	Key features
<i>Candida</i>	'Cottage cheese' discharge Vulvitis Itch
<i>Trichomonas vaginalis</i>	Offensive, yellow/green, frothy discharge Vulvovaginitis Strawberry cervix
Bacterial vaginosis	Offensive, thin, white/grey, 'fishy' discharge

**Question 141 of 167**

Next

A 34-year-old man is diagnosed as being HIV positive. He was born and brought up in the United Kingdom and is currently fit and well with no past medical history. At what point should anti-retroviral therapy be started?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. At the time of diagnosis  |
| <input type="radio"/> | B. $CD4 < 200 \times 10^6/l$ |
| <input type="radio"/> | C. $CD4 < 250 \times 10^6/l$ |
| <input type="radio"/> | D. $CD4 < 300 \times 10^6/l$ |
| <input type="radio"/> | E. $CD4 < 350 \times 10^6/l$ |

Next question

Start anti-retrovirals in HIV when  $CD4 < 350 \times 10^6/l$

Anti-retroviral therapy has previously been delayed until CD4 counts were below  $200 \times 10^6/l$ . This was largely due to the toxicity of drugs and fear of resistance developing. Recent guidelines now suggest starting treatment when counts drop below  $350 \times 10^6/l$

**HIV: anti-retrovirals**

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

**Nucleoside analogue reverse transcriptase inhibitors (NRTI)**

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

**Non-nucleoside reverse transcriptase inhibitors (NNRTI)**

- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

**Protease inhibitors (PI)**

- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system



You are counselling a 26-year-old man who has recently had a positive HIV test. His most recent CD4 count is 650 cells/mm<sup>3</sup>. Which one of the following vaccinations is contraindicated?

- ☐ A. Oral poliomyelitis
- ☐ B. Yellow fever
- ☐ C. Pneumococcus
- ☐ D. Parenteral poliomyelitis
- ☐ E. Measles, Mumps, Rubella

[Next question](#)

### HIV: immunisation

The Department of Health 'Greenbook' on immunisation defers to the British HIV Association for guidelines relating to immunisation of HIV-infected adults

Vaccines that can be used in all HIV-infected adults	Vaccines that can be used if CD4 > 200	Contraindicated in HIV-infected adults
Hepatitis A Hepatitis B <i>Haemophilus influenzae</i> B (Hib) Influenza-parenteral Japanese encephalitis Meningococcus-MenC Meningococcus-ACWY I Pneumococcus-PPV23 Poliomyelitis-parenteral (IPV) Rabies Tetanus-Diphtheria (Td)	Measles, Mumps, Rubella (MMR) Varicella Yellow Fever	Cholera CVD103-HgR Influenza-intranasal Poliomyelitis-oral (OPV) Tuberculosis (BCG)

A 62-year-old female with chronic renal failure (GFR = 35 ml/min) is diagnosed as having pulmonary tuberculosis. What changes need to be made to her anti-tuberculosis regime given her renal impairment?

<input type="radio"/>	A. Reduction in isoniazid dose
<input type="radio"/>	B. Reduction in rifampicin dose
<input type="radio"/>	C. Reduction in pyrazinamide dose
<input type="radio"/>	D. Reduction in ethambutol dose
<input type="radio"/>	E. No changes

[Next question](#)

### Tuberculosis: drug side-effects

Common side effects:

Rifampicin

- potent liver enzyme inducer
- hepatitis, orange secretions
- flu-like symptoms

Isoniazid

- peripheral neuropathy: prevent with pyridoxine (Vitamin B6)
- hepatitis, agranulocytosis
- liver enzyme inhibitor

Pyrazinamide

- hyperuricaemia causing gout
- hepatitis

Ethambutol

- optic neuritis: check visual acuity before and during treatment
- dose needs adjusting in patients with renal impairment

A 63-year-old man who migrated from India 7 months ago is referred to the acute medical unit with a history of headache and pyrexia. A lumbar puncture suggests a diagnosis of meningeal tuberculosis. What treatment should he be started on?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Rifampicin, isoniazid, pyrazinamide and ethambutol                   |
| <input type="radio"/> | B. Rifampicin and streptomycin  |
| <input type="radio"/> | C. Rifampicin, isoniazid, pyrazinamide, ethambutol and streptomycin     |
| <input type="radio"/> | D. Rifampicin and isoniazid with prednisolone                           |
| <input type="radio"/> | E. Rifampicin, isoniazid, pyrazinamide and ethambutol with prednisolone |

Next question

The use of steroids in patients with tuberculous meningitis is supported by a Cochrane review in 2008

### Tuberculosis: drug therapy

The standard therapy for treating **active tuberculosis** is:

Initial phase - first 2 months (RIPE)

- Rifampicin
- Isoniazid
- Pyrazinamide
- Ethambutol (the 2006 NICE guidelines now recommend giving a 'fourth drug' such as ethambutol routinely - previously this was only added if drug-resistant tuberculosis was suspected)

Continuation phase - next 4 months

- Rifampicin
- Isoniazid

The treatment for **latent tuberculosis** is isoniazid alone for 6 months

Patients with **meningeal tuberculosis** are treated for a prolonged period (at least 12 months) with the addition of steroids

**Directly observed therapy** with a three times a week dosing regimen may be indicated in certain groups, including:

- homeless people with active tuberculosis
- patients who are likely to have poor concordance
- all prisoners with active or latent tuberculosis

A 39-year-old female who has recently emigrated from sub-Saharan Africa is screened for tuberculosis. She reports being fit and well with no past medical history and has never had a BCG vaccination. Her chest x-ray is normal so she has a Mantoux test which is positive. An interferon gamma test is also performed which is positive. A HIV test is requested which is negative. What treatment would you recommend?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Isoniazid for 6 months  |
| <input type="radio"/> | B. Rifampicin, isoniazid, pyrazinamide and ethambutol for 6 months   |
| <input type="radio"/> | C. Observe   |
| <input type="radio"/> | D. Rifampicin, isoniazid, pyrazinamide and ethambutol for 2 months then step down to rifampicin and isoniazid for 4 months |
| <input type="radio"/> | E. Rifampicin and isoniazid for 6 months   |

[Next question](#)

This patient has latent tuberculosis

### Tuberculosis: drug therapy

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- homeless people with active tuberculosis
- patients who are likely to have poor concordance
- all prisoners with active or latent tuberculosis

A 12-year-old girl is prescribed oseltamivir for suspected influenza. What is the mechanism of action of oseltamivir?

<input type="radio"/>	A. Inhibits RNA polymerase
<input type="radio"/>	B. Interferes with the capping of viral mRNA
<input type="radio"/>	C. Neuraminidase inhibitor
<input type="radio"/>	D. Inhibits DNA polymerase
<input type="radio"/>	E. Protease inhibitor

Next question

## H1N1 influenza pandemic

The 2009 H1N1 influenza (swine flu) outbreak was first observed in Mexico in early 2009. In June 2009, the WHO declared the outbreak to be a pandemic.

### H1N1

The H1N1 virus is a subtype of the influenza A virus and the most common cause of flu in humans. The 2009 pandemic was caused by a new strain of the H1N1 virus.

The following groups are particularly at risk:

- patients with chronic illnesses and those on immunosuppressants
- pregnant women
- young children under 5 years old

### Features

The majority of symptoms are typical of those seen in a flu-like illness:

- fever greater than 38°C
- myalgia
- lethargy
- headache
- rhinitis
- sore throat
- cough
- diarrhoea and vomiting

A minority of patients may go on to develop an acute respiratory distress syndrome which may require ventilatory

support.

## **Treatment**

There are two main treatments currently available:

### Oseltamivir (Tamiflu)

- oral medication
- a neuraminidase inhibitor which prevents new viral particles from being released by infected cells
- common side-effects include nausea, vomiting, diarrhoea and headaches

### Zanamivir (Relenza)

- inhaled medication\*
- also a neuraminidase inhibitor
- may induce bronchospasm in asthmatics

\*intravenous preparations are available for patients who are acutely unwell

A 29-year-old HIV positive man is admitted with right-sided hemiplegia. For the past four days he has been complaining of headache and flu-like symptoms. CT scan shows multiple ring enhancing lesions. A diagnosis of cerebral toxoplasmosis is suspected. What is the most suitable management?

<input type="radio"/>	A. Artemether and lumefantrine
<input type="radio"/>	B. Co-trimoxazole
<input type="radio"/>	C. Supportive treatment
<input type="radio"/>	D. Pyrimethamine and sulphadiazine
<input type="radio"/>	E. Metronidazole and gentamicin

[Next question](#)

## Toxoplasmosis

*Toxoplasma gondii* is a protozoa which infects the body via the GI tract, lung or broken skin. It's oocysts release trophozoites which migrate widely around the body including to the eye, brain and muscle. The usual animal reservoir is the cat, although other animals such as rats carry the disease.

Most infections are asymptomatic. Symptomatic patients usually have a self-limiting infection, often having clinical features resembling infectious mononucleosis (fever, malaise, lymphadenopathy). Other less common manifestations include meningoencephalitis and myocarditis.

### Investigation

- antibody test
- Sabin-Feldman dye test

Treatment is usually reserved for those with severe infections or patients who are immunosuppressed

- pyrimethamine plus sulphadiazine for at least 6 weeks

Congenital toxoplasmosis is due to transplacental spread from the mother. It causes a variety of effects to the unborn child including microcephaly, hydrocephalus, cerebral calcification and chorioretinitis.

A 22-year-old female presents with an offensive vaginal discharge. History and examination findings are consistent with a diagnosis of bacterial vaginosis. What is the most appropriate initial management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Oral azithromycin                             |
| <input type="radio"/> | B. Topical hydrocortisone                        |
| <input type="radio"/> | C. Oral metronidazole                            |
| <input type="radio"/> | D. Clotrimazole pessary                          |
| <input type="radio"/> | E. Advice regarding hygiene and cotton underwear |

[Next question](#)

Bacterial vaginosis: oral metronidazole

## Bacterial vaginosis

Bacterial vaginosis (BV) describes an overgrowth of predominately anaerobic organisms such as *Gardnerella vaginalis*. This leads to a consequent fall in lactic acid producing aerobic lactobacilli resulting in a raised vaginal pH.

Whilst BV is not a sexually transmitted infection it is seen almost exclusively in sexually active women.

### Features

- vaginal discharge: 'fishy', offensive
- asymptomatic in 50%

Amsel's criteria for diagnosis of BV - 3 of the following 4 points should be present

- thin, white homogenous discharge
- clue cells on microscopy
- vaginal pH > 4.5
- positive whiff test (addition of potassium hydroxide results in fishy odour)

### Management

- oral metronidazole for 5-7 days
- 70-80% initial cure rate
- relapse rate > 50% within 3 months



- the BNF suggests topical metronidazole or topical clindamycin as alternatives

#### Bacterial vaginosis in pregnancy

- results in an increased risk of preterm labour, low birth weight and chorioamnionitis, late miscarriage
- it was previously taught that oral metronidazole should be avoided in the first trimester and topical clindamycin used instead. Recent guidelines however recommend that oral metronidazole is used throughout pregnancy. The BNF still advises against the use of high dose metronidazole regimes

A 29-year-old woman presents to the genitourinary medicine clinic for treatment of recurrent genital warts. Which one the following viruses are most likely to be responsible?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Human papilloma virus 16 & 18 |
| <input type="radio"/> | B. Human papilloma virus 13 & 17 |
| <input type="radio"/> | C. Human papilloma virus 6 & 11  |
| <input type="radio"/> | D. Human papilloma virus 12 & 14 |
| <input type="radio"/> | E. Human papilloma virus 15 & 21 |

[Next question](#)

Genital warts - 90% are caused by HPV 6 & 11

Types 6 and 11 are responsible for 90% of genital warts cases

### Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

#### Features

- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

#### Management

- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment and recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

Which one of the following vaccines uses an inactivated preparation of the organism or virus?

<input type="radio"/>	A. Tetanus
<input type="radio"/>	B. Meningococcus
<input type="radio"/>	C. Oral polio
<input checked="" type="radio"/>	D. Rabies
<input type="radio"/>	E. Diphtheria

Next question

## Vaccinations

It is important to be aware of vaccines which are of the live-attenuated type as these may pose a risk to immunocompromised patients. The main types of vaccine are as follows:

### Live attenuated

- BCG
- measles, mumps, rubella (MMR)
- oral polio
- yellow fever
- oral typhoid\*

### Inactivated preparations

- rabies
- influenza

### Detoxified exotoxins

- tetanus

### Extracts of the organism/virus (sometimes termed fragment)\*\*

- diphtheria
- pertussis ('acellular' vaccine)
- hepatitis B
- meningococcus, pneumococcus, haemophilus

## Notes

- influenza: different types are available, including whole inactivated virus, split virion (virus particles disrupted by detergent treatment) and sub-unit (mainly haemagglutinin and neuraminidase)
- cholera: contains inactivated Inaba and Ogawa strains of *Vibrio cholerae* together with recombinant B-subunit of the cholera toxin
- hepatitis B: contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology

\*whole cell typhoid vaccine is no longer used in the UK

\*\*may also be produced using recombinant DNA technology

Which one of the following congenital infections is most characteristically associated with chorioretinitis?

- ☐ A. Cytomegalovirus
- ☐ B. *Treponema pallidum*
- ☐ C. Rubella
- ☐ D. *Toxoplasma gondii*
- ☐ E. Parvovirus B19

Next question

#### Congenital toxoplasmosis

- cerebral calcification
- chorioretinitis

A form of 'salt and pepper' chorioretinitis is also seen in congenital rubella but this is not a common feature.

Chorioretinitis is found in around 75% of patients with congenital toxoplasmosis.

#### Congenital infections

The major congenital infections encountered in examinations are rubella, toxoplasmosis and cytomegalovirus

Cytomegalovirus is the most common congenital infection in the UK. Maternal infection is usually asymptomatic

	Rubella	Toxoplasmosis	Cytomegalovirus
<b>Characteristic features</b>	Sensorineural deafness Congenital cataracts Congenital heart disease (e.g. patent ductus arteriosus) Glaucoma	Cerebral calcification Chorioretinitis Hydrocephalus	Growth retardation Purpuric skin lesions
<b>Other features</b>	Growth retardation Hepatosplenomegaly Purpuric skin lesions 'Salt and pepper' chorioretinitis Microphthalmia Cerebral palsy	Anaemia Hepatosplenomegaly Cerebral palsy	Sensorineural deafness Encephalitis Pneumonitis Hepatosplenomegaly Anaemia Jaundice Cerebral palsy

### Question 152 of 167

Infection with *Schistosoma haematobium* is most strongly associated with:

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Transitional cell bladder cancer |
| <input type="radio"/> | B. Lung cancer                      |
| <input type="radio"/> | C. Hepatoma                         |
| <input type="radio"/> | D. Vulval carcinoma                 |
| <input type="radio"/> | E. Squamous cell bladder cancer     |

[Next question](#)

Schistosomiasis is a risk factor for **Squamous cell bladder cancer**

### Schistosomiasis

Schistosomiasis, or bilharzia, is a parasitic flatworm infection. The following types of schistosomiasis are recognised:

- *Schistosoma mansoni* and *Schistosoma intercalatum*: intestinal schistosomiasis
- *Schistosoma haematobium*: urinary schistosomiasis

### *Schistosoma haematobium*

This typically presents as a 'swimmer's itch' in patients who have recently returned from Africa. *Schistosoma haematobium* is a risk factor for squamous cell bladder cancer

#### Features

- frequency
- haematuria
- bladder calcification

#### Management

- single oral dose of praziquantel

Which of the following is least recognised as a cause of a false positive VDRL test?

<input type="radio"/>	A. Pregnancy
<input type="radio"/>	B. SLE
<input type="radio"/>	C. Oral contraceptive pill
<input type="radio"/>	D. Tuberculosis
<input type="radio"/>	E. HIV

Next question

### Syphilis: investigation

*Treponema pallidum* is a very sensitive organism and cannot be grown on artificial media. The diagnosis is therefore usually based on clinical features, serology and microscopic examination of infected tissue

Serological tests can be divided into

- cardiolipin tests (not treponeme specific)
- treponemal specific antibody tests

Cardiolipin tests

- syphilis infection leads to the production of non-specific antibodies that react to cardiolipin
- examples include VDRL (Venereal Disease Research Laboratory) & RPR (rapid plasma reagin)
- insensitive in late syphilis
- becomes negative after treatment

Treponemal specific antibody tests

- example: TPHA (*Treponema pallidum* HaemAgglutination test)
- remains positive after treatment

Causes of false positive cardiolipin tests

- pregnancy
- SLE, anti-phospholipid syndrome
- TB
- leprosy
- malaria
- HIV

A man develops vomiting and abdominal pain 2 hours after leaving a Chinese restaurant. What is the most likely causative organism?

- ☐ A. *Escherichia coli*
- ☐ B. *Shigella*
- ☐ C. *Staphylococcus aureus*
- ☐ D. *Bacillus cereus*
- ☐ E. *Clostridium perfringens*

[Next question](#)

The obvious clue in this question is the short incubation period - this points to a diagnosis of *Staphylococcus aureus* or *Bacillus cereus*. *Bacillus cereus* infection is often associated with Chinese restaurants due to the link with rice

There are two recognised types of *Bacillus cereus* infection. The first type produces a vomiting illness and has an incubation period of 1-6 hours. The second type produces a diarrhoeal illness with an incubation period of 6-14 hours.

### Gastroenteritis

Gastroenteritis may either occur whilst at home or whilst travelling abroad (travellers' diarrhoea)

Travellers' diarrhoea may be defined as at least 3 loose to watery stools in 24 hours with or without one of more of abdominal cramps, fever, nausea, vomiting or blood in the stool. The most common cause is *Escherichia coli*

Another pattern of illness is 'acute food poisoning'. This describes the sudden onset of nausea, vomiting and diarrhoea after the ingestion of a toxin. Acute food poisoning is typically caused by *Staphylococcus aureus*, *Bacillus cereus* or *Clostridium perfringens*.

### Stereotypical histories

<b><i>Escherichia coli</i></b>	Common amongst travellers Watery stools Abdominal cramps and nausea
<b>Giardiasis</b>	Prolonged, non-bloody diarrhoea
<b>Cholera</b>	Profuse, watery diarrhoea Severe dehydration resulting in weight loss Not common amongst travellers
<b><i>Shigella</i></b>	Bloody diarrhoea Vomiting and abdominal pain
<b><i>Staphylococcus aureus</i></b>	Severe vomiting Short incubation period



<b><i>Campylobacter</i></b>	<p>A flu-like prodrome is usually followed by crampy abdominal pains, fever and diarrhoea which may be bloody</p> <p>Complications include Guillain-Barre syndrome</p>
<b><i>Bacillus cereus</i></b>	<p>Two types of illness are seen</p> <ul style="list-style-type: none"> <li>• vomiting within 6 hours, stereotypically due to rice</li> <li>• diarrhoeal illness occurring after 6 hours</li> </ul>
<b>Amoebiasis</b>	Gradual onset bloody diarrhoea, abdominal pain and tenderness which may last for several weeks

#### Incubation period

- 1-6 hrs: *Staphylococcus aureus*, *Bacillus cereus*\*
- 12-48 hrs: *Salmonella*, *Escherichia coli*
- 48-72 hrs: *Shigella*, *Campylobacter*
- > 7 days: Giardiasis, Amoebiasis

\*vomiting subtype, the diarrhoeal illness has an incubation period of 6-14 hours

A 34-year-old man from Venezuela presents with a flu-like illness and periorbital oedema. Generalised lymphadenopathy is noted. A diagnosis of Chagas' disease is confirmed on blood smear. What is the most appropriate treatment?

<input type="radio"/>	A. Benznidazole
<input type="radio"/>	B. Sodium stibogluconate
<input type="radio"/>	C. Metronidazole
<input type="radio"/>	D. Pentamidine
<input type="radio"/>	E. Atovaquone-proguanil

Next question

### Trypanosomiasis

Two main form of this protozoal disease are recognised - African trypanosomiasis (sleeping sickness) and American trypanosomiasis (Chagas' disease)

Two forms of **African trypanosomiasis**, or **sleeping sickness**, are seen - *Trypanosoma gambiense* in West Africa and *Trypanosoma rhodesiense* in East Africa. Both types are spread by the tsetse fly. *Trypanosoma rhodesiense* tends to follow a more acute course. Clinical features include:

- Trypanosoma chancre - tender subcutaneous nodule at site of infection
- enlargement of posterior cervical lymph nodes
- later: central nervous system involvement e.g. meningoencephalitis

#### Management

- early disease: IV pentamidine or suramin
- later disease or central nervous system involvement: IV melarsoprol

**American trypanosomiasis**, or **Chagas' disease**, is caused by the protozoan *Trypanosoma cruzi*. The vast majority of patients (95%) are asymptomatic in the acute phase although a chagoma (an erythematous nodule at site of infection) and periorbital oedema are sometimes seen. Chronic Chagas' disease mainly affects the heart and gastrointestinal tract

- myocarditis may lead to heart failure and arrhythmias
- gastrointestinal features includes megaesophagus and megacolon causing dysphagia and constipation

#### Management

- treatment is most effective in the acute phase using azole or nitroderivatives such as benznidazole or nifurtimox
- chronic disease management involves treating the complications e.g., heart failure

A 48-year-old salesman presents with a 5 day history of cough and pleuritic chest pain. He has no past medical history of note. On examination his temperature is 38.2°C, blood pressure is 120/80 mmHg, respiratory rate 18/min and pulse 84/min. Auscultation of the chest reveals bronchial breathing in the left base and the same area is dull to percussion. What is the most suitable management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Oral amoxicillin + discharge                |
| <input type="radio"/> | B. Oral co-amoxiclav + discharge               |
| <input type="radio"/> | C. Oral amoxicillin + erythromycin + discharge |
| <input type="radio"/> | D. Oral erythromycin + discharge               |
| <input type="radio"/> | E. Admit                                       |

Next question

### Pneumonia: community-acquired

Community acquired pneumonia (CAP) may be caused by the following infectious agents:

- *Streptococcus pneumoniae* (accounts for around 80% of cases)
- *Haemophilus influenzae*
- *Staphylococcus aureus*: commonly after the 'flu
- atypical pneumonias (e.g. Due to *Mycoplasma pneumoniae*)
- viruses

*Klebsiella pneumoniae* is classically in alcoholics

***Streptococcus pneumoniae* (pneumococcus)** is the most common cause of community-acquired pneumonia

Characteristic features of pneumococcal pneumonia

- rapid onset
- high fever
- pleuritic chest pain
- herpes labialis

### Management

The British Thoracic Society published guidelines in 2009:

- low or moderate severity CAP: oral amoxicillin. A macrolide should be added for patients admitted to hospital
- high severity CAP: intravenous co-amoxiclav + clarithromycin OR cefuroxime + clarithromycin OR cefotaxime + clarithromycin

What is the first line treatment in hydatid disease?

<input type="radio"/>	A. Metronidazole
<input type="radio"/>	B. Ciprofloxacin
<input type="radio"/>	C. Itraconazole
<input checked="" type="radio"/>	D. Albendazole
<input type="radio"/>	E. Sodium stibogluconate

Next question

## Tape worms

Tape worms are made up of repeated segments called proglottids. These are often present in faeces and are useful diagnostically

### Cysticercosis

- caused by *Taenia solium* (from pork) and *Taenia saginata* (from beef)
- management: niclosamide

### Hydatid disease

- caused by the dog tapeworm *Echinococcus granulosus*
- life-cycle involves dogs ingesting hydatid cysts from sheep liver
- often seen in farmers
- may cause liver cysts
- management: albendazole

Which one of the following is least likely to result from *Streptococcus pyogenes* infection?

<input type="radio"/>	A. Rheumatic fever
<input type="radio"/>	B. Scarlet fever
<input type="radio"/>	C. Cellulitis
<input type="radio"/>	D. Type 2 necrotizing fasciitis
<input type="radio"/>	E. Pneumonia

Next question

*Streptococcus pyogenes* rarely causes pneumonia.

## Streptococci

Streptococci are gram-positive cocci. They may be divided into alpha and beta haemolytic types

### Alpha haemolytic streptococci (partial haemolysis)

The most important alpha haemolytic *Streptococcus* is *Streptococcus pneumoniae* (pneumococcus). Pneumococcus is a common cause of pneumonia, meningitis and otitis media. Another clinical example is *Streptococcus viridans*

### Beta haemolytic streptococci (complete haemolysis)

These can be subdivided into groups A-H. Only groups A, B & D are important in humans.

#### Group A

- most important organism is *Streptococcus pyogenes*
- responsible for erysipelas, impetigo, cellulitis, type 2 necrotizing fasciitis and pharyngitis/tonsillitis
- immunological reactions can cause rheumatic fever or post-streptococcal glomerulonephritis
- erythrogenic toxins cause scarlet fever

#### Group B

- *Streptococcus agalactiae* may lead to neonatal meningitis and septicaemia

#### Group D

- *Enterococcus*

Which one of the following organisms is most contagious?

<input type="radio"/>	A. Varicella zoster virus
<input type="radio"/>	B. Epstein Barr virus
<input type="radio"/>	C. Rotavirus
<input type="radio"/>	D. Herpes simplex virus
<input type="radio"/>	E. <i>Haemophilus influenzae</i>

Next question

## Chickenpox

Chickenpox is caused by primary infection with varicella zoster virus. Shingles is reactivation of dormant virus in dorsal root ganglion

Chickenpox is highly infectious

- spread via the respiratory route
- can be caught from someone with shingles
- infectivity = 4 days before rash, until 5 days after the rash first appeared\*
- incubation period = 10-21 days

Clinical features (tend to be more severe in older children/adults)

- fever initially
- itchy, rash starting on head/trunk before spreading. Initially macular then papular then vesicular
- systemic upset is usually mild

Management is supportive

- keep cool, trim nails
- calamine lotion
- school exclusion: current HPA advice is 5 days from start of skin eruption. They also state 'Traditionally children have been excluded until all lesions are crusted. However, transmission has never been reported beyond the fifth day of the rash.'
- immunocompromised patients and newborns with peripartum exposure should receive varicella zoster immunoglobulin (VZIG). If chickenpox develops then IV aciclovir should be considered

A common complication is secondary bacterial infection of the lesions. Rare complications include

- pneumonia
- encephalitis (cerebellar involvement may be seen)
- disseminated haemorrhagic chickenpox
- arthritis, nephritis and pancreatitis may very rarely be seen

\*it was traditionally taught that patients were infective until all lesions had scabbed over

A 50-year-old sewage worker presents with a one week history of fever and feeling generally unwell. Which one of the following features would be least consistent with a diagnosis of leptospirosis?

<input type="radio"/>	A. Meningism
<input type="radio"/>	B. Conjunctival erythema
<input type="radio"/>	C. Productive cough
<input type="radio"/>	D. Decreased urine output
<input type="radio"/>	E. Severe myalgia

[Next question](#)

Pulmonary complications can occur in leptospirosis but generally happen in severe and late-stage disease. Severe disease may result in acute respiratory distress syndrome or pulmonary haemorrhage.

### Leptospirosis

Also known as Weil's disease\*, leptospirosis is commonly seen in questions referring to sewage workers, farmers, vets or people who work in abattoir. It is caused by the spirochaete *Leptospira interrogans* (serogroup L icterohaemorrhagiae), classically being spread by contact with infected rat urine. Weil's disease should always be considered in high-risk patients with hepatorenal failure

#### Features

- fever
- flu-like symptoms
- renal failure (seen in 50% of patients)
- jaundice
- subconjunctival haemorrhage
- headache, may herald the onset of meningitis

#### Management

- high-dose benzylpenicillin or doxycycline

\*the term Weil's disease is sometimes reserved for the most severe 10% of cases that are associated with jaundice



**Question 161 of 167**

Next

A 33-year-old man presents 6 weeks after visiting North Africa on business. He describes feeling lethargic, abdominal pain and having episodic fever. A blood screen is sent which reveals the following:

Hb	15.9 g/dl
WBC	7.1 *10 <sup>9</sup> /l
Platelets	343 *10 <sup>9</sup> /l
Bilirubin	53 µmol/l
ALP	169 u/l
ALT	364 u/l
Hepatitis A IgM	Negative
HBsAg	Negative

What is the most likely diagnosis?

- ☐ A. Infectious mononucleosis
- ☐ B. Hepatitis B
- ☐ C. Hepatitis C
- ☐ D. HIV
- ☐ E. Hepatitis E

Next question

The incubation period and negative HBsAg points to a diagnosis of Hepatitis E.

**Hepatitis E****Overview**

- RNA virus
- spread by the faecal-oral route, incubation period = 3-8 weeks
- common in Central and South-East Asia, North and West Africa, and in Mexico
- causes a similar disease to hepatitis A, but carries a significant mortality (about 20%) during pregnancy
- does not cause chronic disease
- a vaccine is currently in development\*, but is not yet in widespread use

\*New England Journal of Medicine 356:895, 2007

What is the most appropriate antibiotic to use in cholera?

<input type="radio"/>	A. Erythromycin
<input type="radio"/>	B. Metronidazole
<input type="radio"/>	C. Doxycycline
<input type="radio"/>	D. Penicillin V
<input type="radio"/>	E. Trimethoprim

Next question

## Cholera

### Overview

- caused by *Vibrio cholerae* - Gram negative bacteria

### Features

- profuse 'rice water' diarrhoea
- dehydration
- hypoglycaemia

### Management

- oral rehydration therapy
- antibiotics: doxycycline, ciprofloxacin

A 17-year-old man attends the local sexual health clinic. He has developed a large, keratinised genital wart on the shaft of his penis. This has been present for around three months but he has been too embarrassed to present before now. What is the most appropriate initial management?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Topical aciclovir      |
| <input type="radio"/> | B. Cryotherapy            |
| <input type="radio"/> | C. Topical salicylic acid |
| <input type="radio"/> | D. Electrocautery         |
| <input type="radio"/> | E. Topical podophyllum    |

[Next question](#)

#### Genital wart treatment

- multiple, non-keratinised warts: topical podophyllum
- solitary, keratinised warts: cryotherapy

As the wart is keratinised cryotherapy should be used initially

#### Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16,18 & 33) predisposes to cervical cancer.

#### Features

- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

#### Management

- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment and recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

A 24-year-old man is admitted to the Emergency Department with breathing difficulties and confusion three weeks after returning from a holiday in Cambodia. His partner says he has had 'the flu' for the past two weeks. A blood film is positive for malarial parasites and a chest x-ray and arterial blood gases suggest acute respiratory distress syndrome. A diagnosis of severe falciparum malaria is suspected. What is the treatment of choice?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Intravenous artesunate                                 |
| <input type="radio"/> | B. Intravenous clindamycin + oral artemether-lumefantrine |
| <input type="radio"/> | C. Intravenous artemether-lumefantrine                    |
| <input type="radio"/> | D. Oral atovaquone-proguanil                              |
| <input type="radio"/> | E. Intravenous quinine                                    |

[Next question](#)

Severe falciparum malaria - intravenous artesunate

## Malaria: Falciparum

### Feature of severe malaria

- schizonts on a blood film
- parasitaemia > 2%
- hypoglycaemia
- temperature > 39 °C
- severe anaemia
- complications as below

### Complications

- cerebral malaria: seizures, coma
- acute renal failure: blackwater fever, secondary to intravascular haemolysis, mechanism unknown
- acute respiratory distress syndrome (ARDS)
- hypoglycaemia
- disseminated intravascular coagulation (DIC)

### Uncomplicated falciparum malaria

- strains resistant to chloroquine are prevalent in certain areas of Asia and Africa

- the 2010 WHO guidelines recommend artemisinin-based combination therapies (ACTs) as first-line therapy
- examples include artemether plus lumefantrine, artesunate plus amodiaquine, artesunate plus mefloquine, artesunate plus sulfadoxine-pyrimethamine, dihydroartemisinin plus piperaquine

#### Severe falciparum malaria

- a parasite counts of more than 2% will usually need parenteral treatment irrespective of clinical state
- intravenous artesunate is now recommended by WHO in preference to intravenous quinine
- if parasite count > 10% then exchange transfusion should be considered
- shock may indicate coexistent bacterial septicaemia - malaria rarely causes haemodynamic collapse

A phlebotomist gives herself a needlestick injury whilst taking blood from a patient who is known to have the HIV infection. What is the chance that the phlebotomist will develop HIV?

- |                       |          |
|-----------------------|----------|
| <input type="radio"/> | A. 0.03% |
| <input type="radio"/> | B. 0.3%  |
| <input type="radio"/> | C. 1%    |
| <input type="radio"/> | D. 3%    |
| <input type="radio"/> | E. 5-10% |

[Next question](#)

The transmission rate of HIV is relatively low compared to hepatitis B and C.

### Post-exposure prophylaxis

#### Hepatitis A

- Human Normal Immunoglobulin (HNIG) or hepatitis A vaccine may be used depending on the clinical situation

#### Hepatitis B

- HBsAg positive source: if the person exposed is a known responder to HBV vaccine then a booster dose should be given. If they are in the process of being vaccinated or are a non-responder they need to have hepatitis B immune globulin (HBIG) and the vaccine
- unknown source: for known responders the green book advises considering a booster dose of HBV vaccine. For known non-responders HBIG + vaccine should be given whilst those in the process of being vaccinated should have an accelerated course of HBV vaccine

#### Hepatitis C

- monthly PCR - if seroconversion then interferon +/- ribavirin

#### HIV

- a combination of oral antiretrovirals (e.g. Tenofovir, emtricitabine, lopinavir and ritonavir) as soon as possible (i.e. Within 1-2 hours, but may be started up to 72 hours following exposure) for 4 weeks
- serological testing at 12 weeks following completion of post-exposure prophylaxis
- reduces risk of transmission by 80%

Varicella zoster

- VZIG for IgG negative pregnant women/immunosuppressed

**Estimates of transmission risk for single needlestick injury**

Hepatitis B	20-30%
Hepatitis C	0.5-2%
HIV	0.3%

Which one of the following statements regarding hepatitis B is correct?

- ☐ A. Ribavirin is the treatment of choice for chronic hepatitis B
- ☐ B. All patient immunised against hepatitis B require an anti-HBs check to assess their response to the vaccine
- ☐ C. 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine
- ☐ D. The vaccine is of the live-attenuated type
- ☐ E. An anti-HBs level of 20 mIU/ml indicates an adequate response to the vaccine

Next question

Only those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease require an anti-HBs check.

## Hepatitis B

Hepatitis B is a double-stranded DNA virus and is spread through exposure to infected blood or body fluids, including vertical transmission from mother to child. The incubation period is 6-20 weeks.

Immunisation against hepatitis B (please see the Greenbook link for more details)

- contains HBsAg adsorbed onto aluminium hydroxide adjuvant and is prepared from yeast cells using recombinant DNA technology
- most schedules give 3 doses of the vaccine with a recommendation for a one-off booster 5 years following the initial primary vaccination
- at risk groups who should be vaccinated include: healthcare workers, intravenous drug users, sex workers, close family contacts of an individual with hepatitis B, individuals receiving blood transfusions regularly, chronic kidney disease patients who may soon require renal replacement therapy, prisoners, chronic liver disease patients
- around 10-15% of adults fail to respond or respond poorly to 3 doses of the vaccine. Risk factors include age over 40 years, obesity, smoking, alcohol excess and immunosuppression
- testing for anti-HBs is only recommended for those at risk of occupational exposure (i.e. Healthcare workers) and patients with chronic kidney disease. In these patients anti-HBs levels should be checked 1-4 months after primary immunisation
- the table below shows how to interpret anti-HBs levels:

Anti-HBs level (mIU/ml)	Response
> 100	Indicates adequate response, no further testing required. Should still receive booster at 5 years
10 - 100	Suboptimal response - one additional vaccine dose should be given. If immunocompetent no further testing is required
< 10	Non-responder. Test for current or past infection. Give further vaccine course (i.e. 3 doses again) with testing following. If still fails to respond then HBIG would be required for protection if exposed to the virus



## Complications of hepatitis B infection

- chronic hepatitis (5-10%)
- fulminant liver failure (1%)
- hepatocellular carcinoma
- glomerulonephritis
- polyarteritis nodosa
- cryoglobulinaemia

## Management of hepatitis B

- pegylated interferon-alpha used to be the only treatment available. It reduces viral replication in up to 30% of chronic carriers. A better response is predicted by being female, < 50 years old, low HBV DNA levels, non-Asian, HIV negative, high degree of inflammation on liver biopsy
- however due to the side-effects of pegylated interferon it is now used less commonly in clinical practice. Oral antiviral medication is increasingly used with an aim to suppress viral replication (not in dissimilar way to treating HIV patients)
- examples include lamivudine, tenofovir and entecavir

### Question 167 of 167

A 35-year-old man returns from a two week holiday in Italy. He has a 10 day history of rectal bleeding associated with lower back pain. On examination there is a painful swelling of his right knee. What is the most likely diagnosis?

<input type="radio"/>	A. Gonococcal septicaemia
<input type="radio"/>	B. Amoebiasis
<input type="radio"/>	C. Crohn's disease
<input type="radio"/>	D. Tuberculosis
<input type="radio"/>	E. Ulcerative colitis

Gonococcus contracted via anal sex may cause proctitis. The knee swelling seen in this patient is septic arthritis, which is characteristic of the second stage of disseminated gonococcal infection. Proctitis may present with either lower back or rectal pain

### Gonorrhoea

Gonorrhoea is caused by the Gram negative diplococcus *Neisseria gonorrhoea*. Acute infection can occur on any mucous membrane surface, typically genitourinary but also rectum and pharynx. The incubation period of gonorrhoea is 2-5 days

#### Features

- males: urethral discharge, dysuria
- females: cervicitis e.g. leading to vaginal discharge
- rectal and pharyngeal infection is usually asymptomatic

Local complications that may develop include urethral strictures, epididymitis and salpingitis (hence may lead to infertility). Disseminated infection may occur - see below

#### Management

- ciprofloxacin 500mg PO used to be the treatment of choice
- however, there is increased resistance to ciprofloxacin and therefore cephalosporins are now used
- options include cefixime 400mg PO (single dose) or ceftriaxone 250mg IM

Disseminated gonococcal infection (DGI) and gonococcal arthritis may also occur, with gonococcal infection being the most common cause of septic arthritis in young adults. The pathophysiology of DGI is not fully understood but is thought to be due to haematogenous spread from mucosal infection (e.g. Asymptomatic genital infection). Initially there may be a classic triad of symptoms: tenosynovitis, migratory polyarthritis and dermatitis. Later complications include septic arthritis, endocarditis and perihepatitis (Fitz-Hugh-Curtis syndrome)

## Key features of disseminated gonococcal infection

- tenosynovitis
- migratory polyarthritits
- dermatitis (lesions can be maculopapular or vesicular)

**Question 1 of 265**

Next

A 62-year-old is started on allopurinol prophylaxis following his second episode of gout in the past 12 months. What is the mechanism of action of allopurinol?

<input type="radio"/>	A. Promotes excretion of uric acid
<input type="radio"/>	B. Causes the depolymerisation of intracellular microtubules
<input type="radio"/>	C. Uric acid chelator
<input checked="" type="radio"/>	D. Inhibits xanthine oxidase
<input type="radio"/>	E. Xanthine oxidase activator

Next question

Allopurinol inhibits xanthine oxidase

Xanthine oxidase is responsible for the oxidation of 6-mercaptopurine to 6-thiouric acid

**Allopurinol**

Allopurinol is used in the prevention of gout. It works by inhibiting xanthine oxidase

Initiating allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300  $\mu\text{mol/l}$
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol\*

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

\*patients with Lesch-Nyhan syndrome often take allopurinol for life

## Interactions

### Azathioprine

- metabolised to active compound 6-mercaptopurine
- xanthine oxidase is responsible for the oxidation of 6-mercaptopurine to 6-thiouric acid
- allopurinol can therefore lead to high levels of 6-mercaptopurine
- a much reduced dose (e.g. 25%) must therefore be used if the combination cannot be avoided

### Cyclophosphamide

- allopurinol reduces renal clearance, therefore may cause marrow toxicity

## Question 2 of 265

Next

A patient develops a broad complex tachycardia two days following a myocardial infarction. Intravenous amiodarone is given. Which one of the following best describes the mechanism of action of amiodarone?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Blocks potassium channels |
| <input type="radio"/> | B. Shortens QT interval      |
| <input type="radio"/> | C. Blocks sodium channels    |
| <input type="radio"/> | D. Opens sodium channels     |
| <input type="radio"/> | E. Blocks calcium channels   |

Next question

Amiodarone - MOA: blocks potassium channels

### Amiodarone

Amiodarone is a class III antiarrhythmic agent used in the treatment of atrial, nodal and ventricular tachycardias. The main mechanism of action is by blocking potassium channels which inhibits repolarisation and hence prolongs the action potential. Amiodarone also has other actions such as blocking sodium channels (a class I effect)

The use of amiodarone is limited by a number of factors

- long half-life (20-100 days)
- should ideally be given into central veins (causes thrombophlebitis)
- has proarrhythmic effects due to lengthening of the QT interval
- interacts with drugs commonly used concurrently e.g. Decreases metabolism of warfarin
- numerous long-term adverse effects (see below)

Monitoring of patients taking amiodarone

- TFT, LFT, U&E, CXR prior to treatment
- TFT, LFT every 6 months

Adverse effects of amiodarone use

- thyroid dysfunction
- corneal deposits
- pulmonary fibrosis/pneumonitis

- liver fibrosis/hepatitis
- peripheral neuropathy, myopathy
- photosensitivity
- 'slate-grey' appearance
- thrombophlebitis and injection site reactions
- bradycardia

### Question 3 of 265

Next

A 44-year-old Bangladeshi man with a history of mitral stenosis and atrial fibrillation is diagnosed with tuberculosis. He is commenced on anti-tuberculosis therapy. Three weeks after starting treatment his INR has increased to 5.6. Which one of the following medications is most likely to be responsible for this increase?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Pyrazinamide |
| <input type="radio"/> | B. Isoniazid    |
| <input type="radio"/> | C. Rifampicin   |
| <input type="radio"/> | D. Ethambutol   |
| <input type="radio"/> | E. Streptomycin |

Next question

Isoniazid **inhibits** the P450 system

It is important when answering questions relating to liver enzymes to be sure whether the question is asking about induction or inhibition. Drugs causing induction are often well known and candidates may rush to give these as the answer. A raised INR is a result of **inhibited** liver enzymes

#### P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole



- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Which one of the following immunosuppressant drugs inhibits calcineurin in T cells?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Mycophenolate mofetil |
| <input type="radio"/> | B. Basiliximab           |
| <input type="radio"/> | C. Azathioprine          |
| <input type="radio"/> | D. Ciclosporin           |
| <input type="radio"/> | E. Methotrexate          |

Next question

Ciclosporin + tacrolimus - MOA: inhibit calcineurin thus decreasing IL-2

Mycophenolate mofetil inhibits inosine monophosphate dehydrogenase. Azathioprine is metabolised to the active compound mercaptopurine, a purine analogue that inhibits DNA synthesis. Methotrexate is an antimetabolite which inhibits dihydrofolate reductase

### Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphatase that activates various transcription factors in T cells

Adverse effects of ciclosporin (note how everything is increased - fluid, BP,  $K^+$ , hair, gums, glucose)

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- gingival hyperplasia
- tremor
- impaired glucose tolerance

Interestingly for an immunosuppressant, ciclosporin is noted by the BNF to be 'virtually non-myelotoxic'.

### Indications

- following organ transplantation
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- ulcerative colitis
- pure red cell aplasia

**Question 5 of 265**

Next

A 45-year-old man with a history of epilepsy and psychiatric problems is admitted to the Emergency Department with confusion following a seizure earlier in the day. On examination he is noted to have a coarse tremor, blood pressure is 134/86 mmHg, pulse is 84/min and the temperature is 36.7°C. What is the most likely diagnosis?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Carbamazepine overdose         |
| <input type="radio"/> | B. Lithium toxicity               |
| <input type="radio"/> | C. Benzodiazepine toxicity        |
| <input type="radio"/> | D. Tricyclic overdose             |
| <input type="radio"/> | E. Neuroleptic malignant syndrome |

Next question

Lithium: fine tremor in chronic treatment, coarse tremor in acute toxicity

A tricyclic overdose may present with seizures but it does not typical cause a tremor

**Lithium toxicity**

Lithium is mood stabilising drug used most commonly prophylactically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys. Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

**Features of toxicity**

- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

**Management**

- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Which one of the following statements regarding metformin is true?

<input type="radio"/>	A. Should be stopped in a patient admitted with a myocardial infarction
<input type="radio"/>	B. Hypoglycaemia is a recognised adverse effect
<input type="radio"/>	C. May cause a metabolic alkalosis
<input type="radio"/>	D. May aggravate necrobiosis lipoidica diabetorum
<input type="radio"/>	E. Increases vitamin B12 absorption

Metformin should be stopped following a myocardial infarction due to the risk of lactic acidosis. It may be introduced at a later date. Diabetic control may be achieved through the use of a insulin/dextrose infusion (e.g. the DIGAMI regime)

### Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

#### Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

#### Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis\* with severe liver disease or renal failure

#### Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is  $> 130 \mu\text{mol/l}$  and stopping metformin if  $> 150 \mu\text{mol/l}$
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

What is the main mechanism of action of simvastatin?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Bile acid sequestrant                     |
| <input type="radio"/> | B. Decreases hepatic HDL synthesis           |
| <input type="radio"/> | C. Inhibits lipoprotein lipase               |
| <input type="radio"/> | D. Decreases intrinsic cholesterol synthesis |
| <input type="radio"/> | E. Agonists of PPAR-alpha                    |

Next question

Statins inhibit HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

## Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

### Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

### Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk  $\geq 20\%$
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is

especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering\*

	<b>Total cholesterol (mmol/l)</b>	<b>LDL cholesterol</b>
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

\*current NICE guidelines do not recommend a target cholesterol in primary prevention

A 30-year-old woman is admitted to the Emergency Department following a suspected peanut allergy. On examination she has gross facial and tongue oedema. Her oxygen saturations are 97% on room air, pulse is 96 / min and blood pressure is 90/62 mmHg. The paramedics have already gained intravenous access. What is the most appropriate way to give adrenaline in this situation?

- ☐ A. Nebulised
- ☐ B. Subdermally
- ☐ C. Intramuscularly
- ☐ D. Intravenously
- ☐ E. Subcutaneously

The Resuscitation Council guidelines only recommend giving adrenaline intramuscularly, regardless of whether the patient has intravenous access or not.

### Anaphylaxis

Anaphylaxis may be defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction.

Anaphylaxis is one of the few times when you would not have time to look up the dose of a medication. The Resuscitation Council guidelines on anaphylaxis have recently been updated. Adrenaline is by far the most important drug in anaphylaxis and should be given as soon as possible. The recommended doses for adrenaline, hydrocortisone and chlorphenamine are as follows:

	Adrenaline	Hydrocortisone	Chlorphenamine
< 6 months	150 mcg (0.15ml 1 in 1,000)	25 mg	250 mcg/kg
6 months - 6 years	150 mcg (0.15ml 1 in 1,000)	50 mg	2.5 mg
6-12 years	300 mcg (0.3ml 1 in 1,000)	100 mg	5 mg
Adult and child > 12 years	500 mcg (0.5ml 1 in 1,000)	200 mg	10 mg

Adrenaline can be repeated every 5 minutes if necessary. The best site for IM injection is the anterolateral aspect of the middle third of the thigh.

Common identified causes of anaphylaxis

- food (e.g. Nuts) - the most common cause in children
- drugs
- venom (e.g. Wasp sting)

A 41-year-old woman is investigated for hot flushes and night sweats. Bloods show a significantly raised FSH level and her symptoms are attributed to the menopause. Following discussions with the patient she elects to have hormone replacement treatment. What is the most significant risk of prescribing an oestrogen-only preparation rather than a combined oestrogen-progestogen preparation?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Increased risk of venous thromboembolism |
| <input type="radio"/> | B. Increased risk of ovarian cancer         |
| <input type="radio"/> | C. Increased risk of endometrial cancer     |
| <input type="radio"/> | D. Increased risk of breast cancer          |
| <input type="radio"/> | E. Increased risk of colorectal cancer      |

[Next question](#)

HRT: unopposed oestrogen increases risk of endometrial cancer

### Hormone replacement therapy: adverse effects

Hormone replacement therapy (HRT) involves the use of a small dose of oestrogen (combined with a progestogen in women with a uterus) to help alleviate menopausal symptoms.

#### Side-effects

- nausea
- breast tenderness
- fluid retention and weight gain

#### Potential complications

- increased risk of breast cancer: increased by the addition of a progestogen
- increased risk of endometrial cancer: reduced by the addition of a progestogen but not eliminated completely. The BNF states that the additional risk is eliminated if a progestogen is given continuously
- increased risk of venous thromboembolism: increased by the addition of a progestogen
- increased risk of stroke
- increased risk of ischaemic heart disease if taken more than 10 years after menopause

#### Breast cancer



- in the Women's Health Initiative (WHI) study there was a relative risk of 1.26 at 5 years of developing breast cancer
- the increased risk relates to duration of use
- breast cancer incidence is higher in women using combined preparations compared to oestrogen-only preparations
- the risk of breast cancer begins to decline when HRT is stopped and by 5 years it reaches the same level as in women who have never taken HRT

A patient is started on cyclophosphamide for vasculitis associated with Wegener's granulomatosis. Which of the following is most characteristically associated with cyclophosphamide?

- ☐ A. Haemorrhagic cystitis
- ☐ B. Cardiomyopathy
- ☐ C. Ototoxicity
- ☐ D. Alopecia
- ☐ E. Weight gain

[Next question](#)

### Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

Which one of the following statements regarding statin-induced myopathy is incorrect?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Rhabdomyolysis may cause renal failure   |
| <input type="radio"/> | B. Patients with an elevated creatine kinase often have no symptoms                   |
| <input type="radio"/> | C. Female sex is a risk factor  |
| <input type="radio"/> | D. Creatine kinase does not need to be routinely checked prior to commencing a statin |
| <input type="radio"/> | E. Pravastatin is more likely to cause myopathy than simvastatin                      |

Next question

Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)

## Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

### Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
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Current guidelines for lipid lowering\*

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\*current NICE guidelines do not recommend a target cholesterol in primary prevention

A 45-year-old man with a history of depression and gastro-oesophageal reflux disease presents due to a milky discharge from his nipples. The following blood results are obtained:

Prolactin	700 mu/l
-----------	----------

Which one of his medications is most likely to be responsible?

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. Omeprazole     |
| <input type="radio"/> | B. Fluoxetine     |
| <input type="radio"/> | C. Metoclopramide |
| <input type="radio"/> | D. Cimetidine     |
| <input type="radio"/> | E. Amitriptyline  |

Next question

#### Causes of raised prolactin - the p's

- pregnancy
- prolactinoma
- physiological
- polycystic ovarian syndrome
- primary hypothyroidism
- phenothiazines, metoclopramide, domperidone

Selective serotonin reuptake inhibitors such as fluoxetine have rarely been associated with hyperprolactinaemia but the most likely cause in this patient is metoclopramide. Cimetidine is generally associated with gynaecomastia, rather than galactorrhoea.

#### Prolactin and galactorrhoea

Prolactin is secreted by the anterior pituitary gland with release being controlled by a wide variety of physiological factors. Dopamine acts as the primary prolactin releasing inhibitory factor and hence dopamine agonists such as bromocriptine may be used to control galactorrhoea. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

#### Features of excess prolactin

- men: impotence, loss of libido, galactorrhoea
- women: amenorrhoea, galactorrhoea

## Causes of raised prolactin

- prolactinoma
- pregnancy
- oestrogens
- physiological: stress, exercise, sleep
- acromegaly: 1/3 of patients
- polycystic ovarian syndrome
- primary hypothyroidism (due to thyrotrophin releasing hormone (TRH) stimulating prolactin release)

## Drug causes of raised prolactin

- metoclopramide, domperidone
- phenothiazines
- haloperidol
- very rare: SSRIs, opioids

**Question 13 of 265**

Next

A 62-year-old man is commenced on finasteride for symptoms of bladder outflow obstruction. Which one of the following adverse effects is most associated with this treatment?

<input type="radio"/>	A. Alopecia
<input type="radio"/>	B. Gynaecomastia
<input type="radio"/>	C. Prostate cancer
<input type="radio"/>	D. Increased levels of serum prostate specific antigen
<input type="radio"/>	E. Postural hypotension

Next question

**Finasteride**

Finasteride is an inhibitor of 5 alpha-reductase, an enzyme which metabolises testosterone into dihydrotestosterone

**Indications**

- benign prostatic hyperplasia
- male-pattern baldness

**Adverse effects**

- impotence
- decrease libido
- ejaculation disorders
- gynaecomastia and breast tenderness

Finasteride causes decreased levels of serum prostate specific antigen

A 69-year-old man is started on tamsulosin for benign prostatic hyperplasia. Which one of the following best describes the side-effects he may experience?

<input type="radio"/>	A. Urgency + insomnia
<input type="radio"/>	B. Dizziness + postural hypotension
<input type="radio"/>	C. Urinary retention + nausea
<input type="radio"/>	D. Urgency + erectile dysfunction
<input type="radio"/>	E. Erectile dysfunction + reduced libido

### Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition seen in older men.

#### Risk factors

- age: around 50% of 50-year-old men will have evidence of BPH and 30% will have symptoms. Around 80% of 80-year-old men have evidence of BPH
- ethnicity: black > white > Asian

BPH typically presents with lower urinary tract symptoms (LUTS), which may be categorised into:

- voiding symptoms (obstructive): weak or intermittent urinary flow, straining, hesitancy, terminal dribbling and incomplete emptying
- storage symptoms (irritative) urgency, frequency, urgency incontinence and nocturia
- post-micturition: dribbling
- complications: urinary tract infection, retention, obstructive uropathy

#### Management options

- watchful waiting
- medication: alpha-1 antagonists, 5 alpha-reductase inhibitors. The use of combination therapy was supported by the Medical Therapy Of Prostatic Symptoms (MTOPS) trial
- surgery: transurethral resection of prostate (TURP)

Alpha-1 antagonists e.g. tamsulosin, alfuzosin

- decrease smooth muscle tone (prostate and bladder)
- considered first-line, improve symptoms in around 70% of men
- adverse effects: dizziness, postural hypotension, dry mouth, depression



## 5 alpha-reductase inhibitors e.g. finasteride

- block the conversion of testosterone to dihydrotestosterone (DHT), which is known to induce BPH
- unlike alpha-1 antagonists causes a reduction in prostate volume and hence may slow disease progression. This however takes time and symptoms may not improve for 6 months. They may also decrease PSA concentrations by up to 50%
- adverse effects: erectile dysfunction, reduced libido, ejaculation problems, gynaecomastia

A 31-year-old woman presents to the Emergency Department complaining of a headache. She has had 'flu' like symptoms for the past three days with the headache developing gradually yesterday. The headache is described as being 'all over' and is worse on looking at bright light or when bending her neck. On examination her temperature is 38.2°, pulse 96 / min and blood pressure 116/78 mmHg. There is neck stiffness present but no focal neurological signs. On close inspection you notice a number of petechiae on her torso. She has been cannulated and bloods (including cultures) have been taken. What is the most appropriate next step?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. IV cefotaxime                 |
| <input type="radio"/> | B. Arrange a CT head             |
| <input type="radio"/> | C. Perform a lumbar puncture     |
| <input type="radio"/> | D. IV dexamethasone              |
| <input type="radio"/> | E. Intramuscular benzypenicillin |

[Next question](#)

This patient has meningococcal meningitis. They need appropriate intravenous antibiotics immediately. With the advent of modern PCR diagnostic techniques there is no justification for delaying potentially lifesaving treatment by performing a lumbar puncture in patients with suspected meningococcal meningitis.

### Meningitis: management

Investigations suggested by NICE

- full blood count
- CRP
- coagulation screen
- blood culture
- whole-blood PCR
- blood glucose
- blood gas

Lumbar puncture if no signs of raised intracranial pressure

### Management

All patients should be transferred to hospital urgently. If patients are in a pre-hospital setting (for example a GP surgery) and meningococcal disease is suspected then intramuscular benzylpenicillin may be given, as long as this doesn't delay transit to hospital.

BNF recommendations on antibiotics

Initial empirical therapy aged 3 months - 50 years	Intravenous cefotaxime
--	------------------------

Initial empirical therapy aged > 50 years	Intravenous cefotaxime + amoxicillin
Meningococcal meningitis	Intravenous benzylpenicillin or cefotaxime
Pneumococcal meningitis	Intravenous cefotaxime
Meningitis caused by <i>Haemophilus influenzae</i>	Intravenous cefotaxime
Meningitis caused by <i>Listeria</i>	Intravenous amoxicillin + gentamicin

If the patient has a history of immediate hypersensitivity reaction to penicillin or to cephalosporins the BNF recommends using chloramphenicol.

#### Management of contacts

- prophylaxis needs to be offered to household and close contacts of patients affected with meningococcal meningitis
- oral rifampicin or ciprofloxacin may be used
- the risk is highest in the first 7 days but persists for at least 4 weeks
- meningococcal vaccination should be offered when serotype results are available, for close contacts who have not previously been vaccinated

**Question 16 of 265**

Next

A 41-year-old woman is admitted following a deliberate overdose of ethylene glycol. She is confused and unable to give any further history. On examination the pulse is 96 / min, blood pressure is 142/84 mmHg and temperature 37.1°C. Blood tests show:

Na <sup>+</sup>	139 mmol/l
K <sup>+</sup>	4.0 mmol/l
Chloride	104 mmol/l
Bicarbonate	26 mmol/l
Urea	4.0 mmol/l
Creatinine	88 µmol/l

What is the most appropriate management of this patient?

- ☐ A. Ethanol
- ☐ B. Fomepizole
- ☐ C. Haemodialysis
- ☐ D. Haemofiltration
- ☐ E. Dantrolene

Next question

Ethylene glycol toxicity management - fomepizole. Also ethanol / haemodialysis

Fomepizole is now used first-line rather than ethanol in ethylene glycol toxicity. There is no indication for haemodialysis at this stage, as a metabolic acidosis has not yet developed

**Ethylene glycol toxicity**

Ethylene glycol is a type of alcohol used as a coolant or antifreeze

Features of toxicity are divided into 3 stages:

- Stage 1: symptoms similar to alcohol intoxication: confusion, slurred speech, dizziness
- Stage 2: metabolic acidosis with high anion gap and high osmolar gap. Also tachycardia, hypertension
- Stage 3: acute renal failure

Management has changed in recent times

- ethanol has been used for many years
- works by competing with ethylene glycol for the enzyme alcohol dehydrogenase

- this limits the formation of toxic metabolites (e.g. glycoaldehyde and glycolic acid) which are responsible for the haemodynamic/metabolic features of poisoning
- **fomepizole**, an inhibitor of alcohol dehydrogenase, is now used first-line in preference to ethanol
- haemodialysis also has a role in refractory cases

A 78-year-old woman is discharged following a fractured neck of femur. On review she is making good progress but consideration is given to secondary prevention of further fractures. What is the most suitable management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Arrange DEXA scan + start strontium ranelate if T-score < -2.5 SD          |
| <input type="radio"/> | B. Start oral bisphosphonate  |
| <input type="radio"/> | C. Arrange DEXA scan + start oral bisphosphonate if T-score < -1.0 SD         |
| <input type="radio"/> | D. Arrange DEXA scan + start hormone replacement therapy if T-score < -2.5 SD |
| <input type="radio"/> | E. Arrange DEXA scan + start oral bisphosphonate if T-score < -1.5 SD         |

Next question

NICE guidelines support starting bisphosphonates without waiting for a DEXA scan in such scenarios

### Osteoporosis: secondary prevention

NICE guidelines were updated in 2008 on the secondary prevention of osteoporotic fractures in postmenopausal women.

Key points include

- treatment is indicated following osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (a T-score of - 2.5 SD or below). In women aged 75 years or older, a DEXA scan may not be required 'if the responsible clinician considers it to be clinically inappropriate or unfeasible'
- vitamin D and calcium supplementation should be offered to all women unless the clinician is confident they have adequate calcium intake and are vitamin D replete
- alendronate is first-line
- around 25% of patients cannot tolerate alendronate, usually due to upper gastrointestinal problems. These patients should be offered risedronate or etidronate (see treatment criteria below)
- strontium ranelate and raloxifene are recommended if patients cannot tolerate bisphosphonates (see treatment criteria below)

### Treatment criteria for patients not taking alendronate

Unfortunately, a number of complicated treatment cut-off tables have been produced in the latest guidelines for patients who do not tolerate alendronate

Risk factors (for use in the tables below)

- parental history of hip fracture
- alcohol intake of 4 or more units per day
- rheumatoid arthritis

T-scores (SD) at (or below) which risedronate or etidronate is recommended when alendronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50-54	Not indicated	- 3.0	- 2.5
55-59	- 3.0	- 3.0	- 2.5
60-64	- 3.0	- 3.0	- 2.5
65-69	- 3.0	- 2.5	- 2.5
70 or older	- 2.5	- 2.5	- 2.5

T-scores (SD) at (or below) which strontium ranelate or raloxifene is recommended when alendronate and either risedronate or etidronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50-54	Not indicated	- 3.5	- 3.5
55-59	- 4.0	- 3.5	- 3.5
60-64	- 4.0	- 3.5	- 3.5
65-69	- 4.0	- 3.5	- 3.0
70-74	- 3.0	- 3.0	- 2.5
75 or older	- 3.0	- 2.5	- 2.5

## Supplementary notes on treatment

### Bisphosphonates

- alendronate, risedronate and etidronate are all licensed for the prevention and treatment of post-menopausal and glucocorticoid-induced osteoporosis
- all three have been shown to reduce the risk of both vertebral and non-vertebral fractures although alendronate, risedronate may be superior to etidronate in preventing hip fractures
- ibandronate is a once-monthly oral bisphosphonate

### Vitamin D and calcium

- poor evidence base to suggest reduced fracture rates in the general population at risk of osteoporotic fractures - may reduce rates in frail, housebound patients

## Raloxifene - selective oestrogen receptor modulator (SERM)

- has been shown to prevent bone loss and to reduce the risk of vertebral fractures, but has not yet been shown to reduce the risk of non-vertebral fractures
- has been shown to increase bone density in the spine and proximal femur
- may worsen menopausal symptoms
- increased risk of thromboembolic events
- may decrease risk of breast cancer

## Strontium ranelate

- 'dual action bone agent' - increases deposition of new bone by osteoblasts and reduces the resorption of bone by osteoclasts
- strong evidence base, may be second-line treatment in near future
- increased risk of thromboembolic events

## Teriparatide

- recombinant form of parathyroid hormone
- very effective at increasing bone mineral density but role in the management of osteoporosis yet to be clearly defined

## Hormone replacement therapy

- has been shown to reduce the incidence of vertebral fracture and non-vertebral fractures
- due to concerns about increased rates of cardiovascular disease and breast cancer it is no longer recommended for primary or secondary prevention of osteoporosis unless the woman is suffering from vasomotor symptoms

## Hip protectors

- evidence to suggest significantly reduce hip fractures in nursing home patients
- compliance is a problem

## Falls risk assessment

- no evidence to suggest reduced fracture rates
- however, do reduce rate of falls and should be considered in management of high risk patients



Which one of the following side-effects is least recognised in patients taking ciclosporin?

<input type="radio"/>	A. Hypokalaemia
<input type="radio"/>	B. Hyperplasia of the gum
<input type="radio"/>	C. Hypertension
<input type="radio"/>	D. Tremor
<input type="radio"/>	E. Excessive hair growth

Next question

Ciclosporin side-effects: everything is increased - fluid, BP,  $K^+$ , hair, gums, glucose

Hyperkalaemia rather than hypokalaemia is seen with ciclosporin use

### Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphatase that activates various transcription factors in T cells

Adverse effects of ciclosporin (note how everything is increased - fluid, BP,  $K^+$ , hair, gums, glucose)

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- gingival hyperplasia
- tremor
- impaired glucose tolerance

Interestingly for an immunosuppressant, ciclosporin is noted by the BNF to be 'virtually non-myelotoxic'.

### Indications

- following organ transplantation
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- ulcerative colitis
- pure red cell aplasia

A 47-year-old man is reviewed in the smoking cessation clinic. Which one of the following conditions would contraindicate the prescription of bupropion?

<input type="radio"/>	A. History of supraventricular tachycardia
<input type="radio"/>	B. Previous episodes of acute pancreatitis
<input type="radio"/>	C. Epilepsy
<input type="radio"/>	D. Depression
<input type="radio"/>	E. Hypertension

[Next question](#)

Bupropion: contraindicated in epilepsy

## Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

### Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

### Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop
- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)
- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

## Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication

A 72-year-old female known to have osteoporosis is started on alendronate. Which one of the following side-effects is it most important to warn her about?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Sore throat  |
| <input type="radio"/> | B. Heartburn    |
| <input type="radio"/> | C. Headache     |
| <input type="radio"/> | D. Diarrhoea    |
| <input type="radio"/> | E. Palpitations |

[Next question](#)

Bisphosphonates can cause a variety of oesophageal problems

Whilst the development of any new problem following the introduction of a new drug warrants medical review it is particularly important to warn patients starting bisphosphonates about symptoms which could suggest an oesophageal reaction, especially with alendronate

### Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

#### Clinical uses

- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metastases

#### Adverse effects

- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw
- increased risk of atypical stress fractures of the proximal femoral shaft in patients taking alendronate

The BNF suggests the following counselling for patients taking oral bisphosphonates

- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

**Question 21 of 265**

Next

A 65-year-old female is admitted to the Emergency Department following an overdose of a long-acting propranolol preparation. On admission she is bradycardic with a pulse of 36/min and BP 90/50. The bradycardia fails to respond to atropine. What is the most appropriate management?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Temporary cardiac pacing |
| <input type="radio"/> | B. Haemodialysis            |
| <input type="radio"/> | C. Glucagon                 |
| <input type="radio"/> | D. Noradrenaline infusion   |
| <input type="radio"/> | E. Salbutamol infusion      |

Next question

Beta-blocker overdose management: atropine + glucagon

Glucagon has a positive inotropic action on the heart and decreases renal vascular resistance. It is therefore useful in patients with beta-blocker cardiotoxicity

Cardiac pacing should be reserved for patients unresponsive to pharmacological therapy

**Beta-blocker overdose**

## Features

- bradycardia
- hypotension
- heart failure
- syncope

## Management

- if bradycardic then atropine
- in resistant cases glucagon may be used

Haemodialysis is not effective in beta-blocker overdose

A 16-year-old girl is admitted to the Emergency Department late on a Friday night. She is complaining of palpitations and feeling 'unwell'. Her friends state that she has had a bad reaction to the alcohol they've been drinking and deny the use of any illicit substances. On examination she is agitated and clutching her chest. Her pupils are mydriatic and the pulse rate is 108/min, blood pressure 130/90 mmHg. She says that she is going to be sick. Which of the following substances may account for this presentation?

<input type="radio"/>	A. Cannabis
<input type="radio"/>	B. Cocaine
<input type="radio"/>	C. LSD
<input type="radio"/>	D. Heroin
<input type="radio"/>	E. Ketamine

### Cocaine

Cocaine use may cause a wide variety of adverse effects

#### Cardiovascular effects

- myocardial infarction
- both tachycardia and bradycardia may occur
- hypertension
- QRS widening and QT prolongation
- aortic dissection

#### Neurological effects

- seizures
- mydriasis
- hypertonia
- hyperreflexia

#### Psychiatric effects

- agitation
- psychosis
- hallucinations

#### Others

- hyperthermia
- metabolic acidosis
- rhabdomyolysis

**Question 23 of 265**

Next

A 40-year-old woman who is known to be HIV positive is reviewed in the respiratory clinic. She has recently started treatment for tuberculosis and is complaining of a loss of sensation in her hands Which one of the following drugs is most likely to be responsible?

<input type="radio"/>	A. Indinavir
<input type="radio"/>	B. Pyrazinamide
<input type="radio"/>	C. Zidovudine
<input type="radio"/>	D. Streptomycin
<input type="radio"/>	E. Isoniazid

Next question

Isoniazid causes peripheral neuropathy

**Tuberculosis: drug side-effects and mechanism of action****Rifampicin**

- mechanism of action: inhibits bacterial DNA dependent RNA polymerase preventing transcription of DNA into mRNA
- potent liver enzyme inducer
- hepatitis, orange secretions
- flu-like symptoms

**Isoniazid**

- mechanism of action: inhibits mycolic acid synthesis
- peripheral neuropathy: prevent with pyridoxine (Vitamin B6)
- hepatitis, agranulocytosis
- liver enzyme inhibitor

**Pyrazinamide**

- mechanism of action: converted by pyrazinamidase into pyrazinoic acid which in turn inhibits fatty acid synthase (FAS) I
- hyperuricaemia causing gout
- hepatitis

## Ethambutol

- mechanism of action: inhibits the enzyme arabinosyl transferase which polymerizes arabinose into arabinan
- optic neuritis: check visual acuity before and during treatment
- dose needs adjusting in patients with renal impairment



**Question 24 of 265**

Next

A 19-year-old student is admitted after being found friends confused and sweating in her room. She is unable to give a history. On examination temperature is 38.1°C, pulse 108/min, BP 130/70 mmHg and respiratory rate 30/min. Heart sounds are normal but she has bibasal fine inspiratory crackles on her chest.

ABGs on air:

pH	7.28
pCO <sub>2</sub>	2.8 kPa
pO <sub>2</sub>	14.2 kPa

What is the most likely diagnosis?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Paracetamol overdose   |
| <input type="radio"/> | B. Acute pancreatitis     |
| <input type="radio"/> | C. Mycoplasma septicaemia |
| <input type="radio"/> | D. Legionella pneumonia   |
| <input type="radio"/> | E. Aspirin overdose       |

Next question

The mixed respiratory alkalosis and metabolic acidosis in a sweaty, confused patient point towards salicylate overdose. The development of pulmonary oedema suggests severe poisoning and is an indication for haemodialysis

**Salicylate overdose**

A key concept for the exam is to understand that salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis. In children metabolic acidosis tends to predominate

Features

- hyperventilation (centrally stimulates respiration)
- tinnitus
- lethargy
- sweating, pyrexia\*
- nausea/vomiting
- hyperglycaemia and hypoglycaemia
- seizures
- coma

## Treatment

- general (ABC, charcoal)
- urinary alkalization is now rarely used - it is contraindicated in cerebral and pulmonary oedema with most units now proceeding straight to haemodialysis in cases of severe poisoning
- haemodialysis

## Indications for haemodialysis in salicylate overdose

- serum concentration > 700mg/L
- metabolic acidosis resistant to treatment
- acute renal failure
- pulmonary oedema
- seizures
- coma

\*salicylates cause the uncoupling of oxidative phosphorylation leading to decreased adenosine triphosphate production, increased oxygen consumption and increased carbon dioxide and heat production

A 54-year-old man with a history of hypertension comes for review. He currently takes lisinopril 10mg od, simvastatin 40mg on and aspirin 75mg od. His blood pressure is well controlled at 124/76 mmHg but he also mentions that he is due to have a tooth extraction next week. What advice should be given with regards to his aspirin use?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Take aspirin as normal but take tranexamic 1g tds acid 24 hours before and after procedure |
| <input type="radio"/> | B. Stop 72 hours before, restart 24 hours after procedure                                     |
| <input type="radio"/> | C. Stop 24 hours before, restart 12 hours after procedure                                     |
| <input type="radio"/> | D. Take aspirin as normal   |
| <input type="radio"/> | E. Stop 48 hours before, restart 24 hours after procedure                                     |

In the BNF section 'Prescribing in dental practice' it advises that patients in this situation should continue taking anti-platelets as normal

### Aspirin

Aspirin works by blocking the action of both cyclooxygenase-1 and 2. Cyclooxygenase is responsible for prostaglandin, prostacyclin and thromboxane synthesis. The blocking of thromboxane A2 formation in platelets reduces the ability of platelets to aggregate which has led to the widespread use of low-dose aspirin in cardiovascular disease. Until recent guidelines changed all patients with established cardiovascular disease took aspirin if there was no contraindication. Following the 2010 technology appraisal of clopidogrel this is no longer the case\*.

Two recent trials (the Aspirin for Asymptomatic Atherosclerosis and the Antithrombotic Trialists Collaboration) have cast doubt on the use of aspirin in primary prevention of cardiovascular disease. Guidelines have not yet changed to reflect this. However the Medicines and Healthcare products Regulatory Agency (MHRA) issued a drug safety update in January 2010 reminding prescribers that aspirin is not licensed for primary prevention.

What do the *current* guidelines recommend?

- first-line for patients with ischaemic heart disease and following a TIA\*\*

Potentiates

- oral hypoglycaemics
- warfarin
- steroids

\*NICE now recommend clopidogrel first-line following an ischaemic stroke (but not for TIAs) and for peripheral arterial disease

\*\*alongside dipyridamole

Where is the site of action of furosemide?

<input type="radio"/>	A. Proximal collecting duct
<input type="radio"/>	B. Ascending loop of Henle
<input type="radio"/>	C. Descending loop of Henle
<input type="radio"/>	D. Distal collecting duct
<input type="radio"/>	E. Macula densa

Next question

### Loop diuretics

Furosemide and bumetanide are loop diuretics that act by inhibiting the Na-K-Cl cotransporter in the thick ascending limb of the loop of Henle, reducing the absorption of NaCl.

#### Indications

- heart failure: both acute (usually intravenously) and chronic (usually orally)
- resistant hypertension, particularly in patients with renal impairment

#### Adverse effects

- hypotension
- hyponatraemia
- hypokalaemia
- hypochloraemic alkalosis
- ototoxicity
- hypocalcaemia
- renal impairment (from dehydration + direct toxic effect)
- hyperglycaemia (less common than with thiazides)
- gout

A 62-year-old man with a history of hypertension and epilepsy is noted to have gingival hyperplasia on examination in the cardiology clinic. Which one of the following drugs is most likely to be responsible?

<input type="radio"/>	A. Sodium valproate
<input type="radio"/>	B. Lisinopril
<input type="radio"/>	C. Atorvastatin
<input type="radio"/>	D. Nifedipine
<input type="radio"/>	E. Carbamazepine

[Next question](#)

Gingival hyperplasia: phenytoin, ciclosporin, calcium channel blockers and AML

### Gingival hyperplasia

Drug causes of gingival hyperplasia

- phenytoin
- ciclosporin
- calcium channel blockers (especially nifedipine)

Other causes of gingival hyperplasia include

- acute myeloid leukaemia (myelomonocytic and monocytic types)

**Question 28 of 265**

Next

A 40-year-old man with a history of psychiatric problems and epilepsy comes for review. He complains that he is drinking excessive amounts of water and having to urinate frequently. He has not lost any weight and states that he is compliant with his current medications. Blood tests show the following:

Na <sup>+</sup>	145 mmol/l
K <sup>+</sup>	4.1 mmol/l
Urea	6.3 mmol/l
Creatinine	101 µmol/l
Glucose (random)	6.2 mol/l

Which one of the following medications is most likely to be responsible for this presentation?

- ☐ A. Carbamazepine
- ☐ B. Fluoxetine
- ☐ C. Olanzapine
- ☐ D. Sodium valproate
- ☐ E. Lithium

Next question

This patient has probably developed nephrogenic diabetes insipidus secondary to lithium therapy. Polyuria, polydipsia and a high-normal sodium are pointers towards this.

**Diabetes insipidus**

Diabetes insipidus (DI) is a condition characterised by either a deficiency of antidiuretic hormone, ADH, (cranial DI) or an insensitivity to antidiuretic hormone (nephrogenic DI).

**Causes of cranial DI**

- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X
- DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

**Causes of nephrogenic DI**

- genetic: the more common form affects the vasopressin (ADH) receptor, the less common form results from a mutation in the gene that encodes the aquaporin 2 channel
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

## Features

- polyuria
- polydipsia

## Investigation

- high plasma osmolarity, low urine osmolarity
- water deprivation test

**Question 29 of 265**

Next

A 54-year-old patient takes hydrocortisone 20mg in the mornings and 5mg at night for Addison's disease. The endocrinology consultant would like her to take prednisolone instead. What dose of prednisolone should be started?

- |                       |          |
|-----------------------|----------|
| <input type="radio"/> | A. 5 mg  |
| <input type="radio"/> | B. 6 mg  |
| <input type="radio"/> | C. 7 mg  |
| <input type="radio"/> | D. 10 mg |
| <input type="radio"/> | E. 25 mg |

Next question

1mg prednisolone = 4mg hydrocortisone

As 1mg prednisolone equals 4mg hydrocortisone then the actual equivalent daily dose is 6.25mg. This was not given as an option in the exam. It would therefore be better to err on the side of caution and over replace steroid initially to avoid the potential risk of hypoadrenalism

**Steroid doses**

## Equivalence

- 1mg prednisolone = 4mg hydrocortisone
- 1mg dexamethasone = 7mg prednisolone



A 70-year-old man who takes warfarin for atrial fibrillation is found to have an INR of 6.2. Which of the following drugs is he most likely to have recently taken?

<input type="radio"/>	A. Ciprofloxacin
<input type="radio"/>	B. Flucloxacillin
<input type="radio"/>	C. St John's Wort
<input type="radio"/>	D. Carbamazepine
<input type="radio"/>	E. Aspirin

[Next question](#)

Ciprofloxacin is a known inhibitor of the P450 system and hence may cause an increase in INR.

### P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

A 25-year-old female who works in a photograph development laboratory is taken to the Emergency Department due to confusion. On admission she is hypoxic and hypotensive. Cyanide poisoning is suspected following discussion with the local poisons unit. What is the definitive treatment?

<input type="radio"/>	A. Haemodialysis
<input type="radio"/>	B. Hydroxocobalamin
<input type="radio"/>	C. Penicillamine
<input type="radio"/>	D. Ferrous sulphate
<input type="radio"/>	E. Desferioxamine

[Next question](#)

## Cyanide poisoning

Cyanide may be used in insecticides, photograph development and the production of certain metals. Toxicity results from reversible inhibition of cellular oxidising enzymes

### Presentation

- 'classical' features: brick-red skin, smell of bitter almonds
- acute: hypoxia, hypotension, headache, confusion
- chronic: ataxia, peripheral neuropathy, dermatitis

### Management

- supportive measures: 100% oxygen
- definitive: hydroxocobalamin

Which one of the following types of reaction takes place in phase II metabolism of a drug?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Conjugation  |
| <input type="radio"/> | B. Hydrolysis   |
| <input type="radio"/> | C. Reduction    |
| <input type="radio"/> | D. Deamination  |
| <input type="radio"/> | E. Dealkylation |

Next question

#### Drug metabolism

- phase I: oxidation, reduction, hydrolysis
- phase II: conjugation

#### Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

#### First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are needed orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol

- verapamil
- isoprenaline
- testosterone
- hydrocortisone

Questions concerning zero-order kinetics and acetylator status are also common in the exam

### **Zero-order kinetics**

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

### **Acetylator status**

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

A 56-year-old man with a history of epilepsy, atrial fibrillation and ischaemic heart disease is noted to have a rash on his forearms and face in the cardiology clinic. Which one of the following drugs is most likely to be responsible?

<input type="radio"/>	A. Verapamil
<input type="radio"/>	B. Carbamazepine
<input type="radio"/>	C. Amiodarone
<input type="radio"/>	D. Digoxin
<input type="radio"/>	E. Clopidogrel

[Next question](#)

A rash on the forearms and face is typical of a photosensitivity rash

### Drugs causing photosensitivity

Causes of drug-induced photosensitivity

- thiazides
- tetracyclines, sulphonamides, ciprofloxacin
- amiodarone
- NSAIDs e.g. piroxicam
- psoralens
- sulphonylureas

Which one of the following drugs may be cleared by haemodialysis?

<input type="radio"/>	A. Beta-blockers
<input type="radio"/>	B. Tricyclics
<input type="radio"/>	C. Aspirin
<input type="radio"/>	D. Benzodiazepines
<input type="radio"/>	E. Digoxin

Next question

### Haemodialysis in overdose

Drugs that can be cleared with haemodialysis - mnemonic: BLAST

- Barbiturate
- Lithium
- Alcohol (inc methanol, ethylene glycol)
- Salicylates
- Theophyllines (charcoal haemoperfusion is preferable)

Drugs which cannot be cleared with haemodialysis include

- tricyclics
- benzodiazepines
- dextropropoxyphene (Co-proxamol)
- digoxin
- beta-blockers

You are clerking a 67-year-old man who has been admitted with chest pain. His past medical history includes hypertension, angina and he continues to smoke 20 cigarettes / day. Blood tests done in the Emergency Department show the following:

Na <sup>+</sup>	133 mmol/l
K <sup>+</sup>	3.3 mmol/l
Urea	4.5 mmol/l
Creatinine	90 µmol/l

Which one of the following factors is most likely to explain the abnormalities seen in the urea and electrolytes?

- ☐ A. Enalapril therapy
- ☐ B. Felodipine therapy
- ☐ C. Bendroflumethiazide therapy
- ☐ D. His smoking history
- ☐ E. Spironolactone therapy

Next question

Bendroflumethiazide causes both hyponatraemia and hypokalaemia. Spironolactone is associated with hyperkalaemia. His smoking would only be relevant if he had lung cancer cause syndrome of inappropriate ADH secretion - there is no indication of this from the question.

### Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide was in the management of hypertension but recent NICE guidelines now recommend other thiazide-like diuretics such as indapamide and chlortalidone.

#### Common adverse effects

- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

#### Rare adverse effects

- thrombocytopaenia
- agranulocytosis
- photosensitivity rash
- pancreatitis

(An eagle eyed user noticed that this entry is very similar to the Wikipedia one. I can assure you that the material has been cut-and-pasted from passmedicine to Wikipedia, and not vice-versa! Note the English spellings of hyponatraemia etc. Check the Wikipedia 'history' page for more details.)



A patient known to have bipolar disorder presents to the Emergency Department with confusion. Which one of the following drugs is most likely to precipitate lithium toxicity?

<input type="radio"/>	A. Frusemide
<input type="radio"/>	B. Sodium valproate
<input type="radio"/>	C. Digoxin
<input type="radio"/>	D. Sodium bicarbonate
<input type="radio"/>	E. Bendroflumethiazide

[Next question](#)

The BNF states that 'loop diuretics are safer than thiazides' in the interactions section.

### Lithium toxicity

Lithium is mood stabilising drug used most commonly prophylactically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys. Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

#### Features of toxicity

- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

#### Management

- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

A 67-year-old man with lung cancer is currently taking MST 30mg bd for pain relief. What dose of oral morphine solution should he be prescribed for breakthrough pain?

- |                       |          |
|-----------------------|----------|
| <input type="radio"/> | A. 5 mg  |
| <input type="radio"/> | B. 10 mg |
| <input type="radio"/> | C. 15 mg |
| <input type="radio"/> | D. 20 mg |
| <input type="radio"/> | E. 30 mg |

[Next question](#)

Breakthrough dose = 1/6th of daily morphine dose

The total daily morphine dose is  $30 \times 2 = 60$  mg, therefore the breakthrough dose should be one-sixth of this, 10 mg

### Palliative care prescribing: pain

#### NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

#### Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered

#### SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative

- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

## Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

## Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

## Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted. NICE give the following advice on conversion:

- a transdermal fentanyl 12 microgram patch equates to approximately 45 mg oral morphine daily
- a transdermal buprenorphine 20 microgram patch equates to approximately 30 mg oral morphine daily.

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

A 61-year-old man develops aortic regurgitation after taking medication for Parkinson's disease. Which one of the following medications is he most likely to have taken?

<input type="radio"/>	A. Pergolide
<input type="radio"/>	B. Cabergoline
<input type="radio"/>	C. Selegiline
<input type="radio"/>	D. Ropinirole
<input type="radio"/>	E. Amantadine

[Next question](#)

Pergolide is particularly associated with valvular dysfunction.

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline

- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

#### Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

#### COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

#### Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benztropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

A 28-year-old woman who has rheumatoid arthritis is to be started on etanercept injections after failing to respond to methotrexate and sulfasalazine. Which one of the following adverse effects is associated with the use of etanercept?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Triggering Churg-Strauss syndrome |
| <input type="radio"/> | B. Thrombocytosis                    |
| <input type="radio"/> | C. Tendonitis                        |
| <input type="radio"/> | D. Cardiomyopathy                    |
| <input type="radio"/> | E. Reactivation of tuberculosis      |

[Next question](#)

**TNF- $\alpha$  inhibitors may reactivate TB**

### Rheumatoid arthritis: management

The management of rheumatoid arthritis (RA) has been revolutionised by the introduction of disease-modifying therapies in the past decade. NICE has issued a number of technology appraisals on the newer agents and released general guidelines in 2009.

Patients with evidence of joint inflammation should start a combination of disease-modifying drugs (DMARD) as soon as possible. Other important treatment options include analgesia, physiotherapy and surgery.

#### Initial therapy

- in the 2009 NICE guidelines it is recommended that patients with newly diagnosed active RA start a combination of DMARDs (including methotrexate and at least one other DMARD, plus short-term glucocorticoids)

#### DMARDs

- methotrexate is the most widely used DMARD. Monitoring of FBC & LFTs is essential due to the risk of myelosuppression and liver cirrhosis. Other important side-effects include pneumonitis
- sulfasalazine
- leflunomide
- hydroxychloroquine

#### TNF-inhibitors

- the current indication for a TNF-inhibitor is an inadequate response to at least two DMARDs including methotrexate
- etanercept: recombinant human protein, acts as a decoy receptor for TNF- $\alpha$ , subcutaneous administration, can cause demyelination, risks include reactivation of tuberculosis
- infliximab: monoclonal antibody, binds to TNF- $\alpha$  and prevents it from binding with TNF receptors, intravenous administration, risks include reactivation of tuberculosis
- adalimumab: monoclonal antibody, subcutaneous administration

## Rituximab

- anti-CD20 monoclonal antibody, results in B-cell depletion
- two 1g intravenous infusions are given two weeks apart
- infusion reactions are common

## Abatacept

- fusion protein that modulates a key signal required for activation of T lymphocytes
- leads to decreased T-cell proliferation and cytokine production
- given as an infusion
- not currently recommended by NICE

A 49-year-old female asks about hormone replacement therapy (HRT). What is the most compelling indication for starting HRT?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Prevention of ischaemic heart disease          |
| <input type="radio"/> | B. Prevention of osteoporosis                     |
| <input type="radio"/> | C. Reversal of vaginal atrophy                    |
| <input type="radio"/> | D. Control of vasomotor symptoms such as flushing |
| <input type="radio"/> | E. Prevention of Alzheimer's disease              |

[Next question](#)

Main indication for HRT: control of vasomotor symptoms

### Hormone replacement therapy: indications

Hormone replacement therapy (HRT) involves the use of a small dose of oestrogen, combined with a progestogen (in women with a uterus), to help alleviate menopausal symptoms.

The indications for HRT have changed significantly over the past ten years as the long-term risks became apparent, primarily as a result of the Women's Health Initiative (WHI) study.

#### Indications

- vasomotor symptoms such as flushing, insomnia and headaches
- premature menopause: should be continued until the age of 50 years
- osteoporosis: but should only be used as second-line treatment

The main indication is the control of vasomotor symptoms. The other indications such as reversal of vaginal atrophy and prevention of osteoporosis should be treated with other agents as first-line therapies

Other benefits include a reduced incidence of colorectal cancer



A 63-year-old female is brought to the Emergency Department due to a decreased level of consciousness. An urgent CT head is performed as she takes warfarin for atrial fibrillation and shows an intracranial haemorrhage. What is the most appropriate management?

- ☐ A. Protamine sulphate
- ☐ B. IV vitamin K alone
- ☐ C. IV vitamin K + prothrombin complex concentrate
- ☐ D. Fresh frozen plasma alone
- ☐ E. IV vitamin K + fresh frozen plasma

As fresh frozen plasma takes time to defrost prothrombin complex concentrate (PCC) should be used in such an urgent situation. The use of PCC is currently limited by availability

### Warfarin overdose

The following is based on the BNF guidelines, which in turn take into account the British Committee for Standards in Haematology (BCSH) guidelines. A 2005 update of the BCSH guidelines emphasised the preference of prothrombin complex concentrate over FFP in major bleeding.

<b>Major bleeding</b>	Stop warfarin Give intravenous vitamin K 5mg Prothrombin complex concentrate - if not available then FFP*
<b>INR &gt; 8.0</b> <b>Minor bleeding</b>	Stop warfarin Give intravenous vitamin K 1-3mg Repeat dose of vitamin K if INR still too high after 24 hours Restart warfarin when INR < 5.0
<b>INR &gt; 8.0</b> <b>No bleeding</b>	Stop warfarin Give oral vitamin K 1-5mg Repeat dose of vitamin K if INR still too high after 24 hours Restart when INR < 5.0
<b>INR 5.0-8.0</b> <b>Minor bleeding</b>	Stop warfarin Give intravenous vitamin K 1-3mg Restart when INR < 5.0
<b>INR 5.0-8.0</b> <b>No bleeding</b>	Withhold 1 or 2 doses of warfarin Reduce subsequent maintenance dose

\*as FFP can take time to defrost prothrombin complex concentrate should be considered in cases of intracranial haemorrhage

### Question 42 of 265

A 52-year-old man with a history of hypertension is found to have a 10-year cardiovascular disease risk of 28%. A decision is made to start simvastatin 40mg on. Liver function tests are performed prior to initialising treatment:

Bilirubin	10 $\mu\text{mol/l}$ (3 - 17 $\mu\text{mol/l}$ )
ALP	96 u/l (30 - 150 u/l)
ALT	30 u/l (10 - 45 u/l)
Gamma-GT	28 u/l (10 - 40 u/l)

Three months later the LFTs are repeated:

Bilirubin	12 $\mu\text{mol/l}$ (3 - 17 $\mu\text{mol/l}$ )
ALP	107 u/l (30 - 150 u/l)
ALT	104 u/l (10 - 45 u/l)
Gamma-GT	76 u/l (10 - 40 u/l)

What is the most appropriate course of action?

- ☐ A. Continue treatment and repeat LFTs in 1 month
- ☐ B. Check creatine kinase
- ☐ C. Reduce dose to simvastatin 10mg on and repeat LFTs in 1 month
- ☐ D. Stop treatment and consider alternative lipid lowering drug
- ☐ E. Stop treatment and refer to gastroenterology

[Next question](#)

Treatment with statins should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range.

### Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

#### Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

## Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk  $\geq 20\%$
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

## Current guidelines for lipid lowering\*

	Total cholesterol (mmol/l)	LDL cholesterol
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

\*current NICE guidelines do not recommend a target cholesterol in primary prevention

Which one of the following drugs is most likely to cause a prolonged QT interval?

<input type="radio"/>	A. Metoclopramide
<input type="radio"/>	B. Verapamil
<input type="radio"/>	C. Ceftriaxone
<input type="radio"/>	D. Sotalol
<input type="radio"/>	E. Digoxin

Next question

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"> <li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li> <li>Romano-Ward syndrome (no deafness)</li> </ul>	<ul style="list-style-type: none"> <li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li> <li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li> <li>methadone</li> <li>chloroquine</li> <li>terfenadine**</li> <li>erythromycin</li> </ul>	<ul style="list-style-type: none"> <li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li> <li>acute myocardial infarction</li> <li>myocarditis</li> <li>hypothermia</li> <li>subarachnoid haemorrhage</li> </ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

## Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

Olanzapine is known to block D2 dopamine receptors. What other type of receptor does it mainly act on?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Alpha-adrenoceptors     |
| <input type="radio"/> | B. Acetylcholine receptors |
| <input type="radio"/> | C. Serotonin receptors     |
| <input type="radio"/> | D. D1 dopamine receptors   |
| <input type="radio"/> | E. H1 histamine receptors  |

Olanzapine, like other atypical antipsychotics, is known to block serotonin receptors (especially the 5-HT<sub>2</sub> subtype) as well as D<sub>2</sub> dopamine receptors

### Atypical antipsychotics

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics

- weight gain
- clozapine is associated with agranulocytosis (see below)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:

- increased risk of stroke (especially olanzapine and risperidone)
- increased risk of venous thromboembolism

Examples of atypical antipsychotics

- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride

Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in patients resistant to other antipsychotic medication

Adverse effects of clozapine

- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients

Which one of the following is not an indication for haemodialysis in salicylate overdose?

<input type="radio"/>	A. Acute renal failure
<input type="radio"/>	B. Seizures
<input type="radio"/>	C. Serum concentration = 400 mg/l
<input type="radio"/>	D. Pulmonary oedema
<input type="radio"/>	E. Metabolic acidosis resistant to treatment

Next question

A serum concentration of greater than 700mg/l is an indication for haemodialysis

### Salicylate overdose

A key concept for the exam is to understand that salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis. In children metabolic acidosis tends to predominate

#### Features

- hyperventilation (centrally stimulates respiration)
- tinnitus
- lethargy
- sweating, pyrexia\*
- nausea/vomiting
- hyperglycaemia and hypoglycaemia
- seizures
- coma

#### Treatment

- general (ABC, charcoal)
- urinary alkalization is now rarely used - it is contraindicated in cerebral and pulmonary oedema with most units now proceeding straight to haemodialysis in cases of severe poisoning
- haemodialysis

#### Indications for haemodialysis in salicylate overdose

- serum concentration > 700mg/L
- metabolic acidosis resistant to treatment
- acute renal failure

- pulmonary oedema
- seizures
- coma

\*salicylates cause the uncoupling of oxidative phosphorylation leading to decreased adenosine triphosphate production, increased oxygen consumption and increased carbon dioxide and heat production



A patient is started on the monoclonal antibody trastuzumab. What is the most likely indication?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Crohn's disease               |
| <input type="radio"/> | B. Chronic lymphocytic leukaemia |
| <input type="radio"/> | C. Renal cancer                  |
| <input type="radio"/> | D. Colorectal cancer             |
| <input type="radio"/> | E. Breast cancer                 |

Next question

Trastuzumab (Herceptin) - monoclonal antibody that acts on the HER2/neu receptor

### Trastuzumab

Trastuzumab (Herceptin) is a monoclonal antibody directed against the HER2/neu receptor. It is used mainly in metastatic breast cancer although some patients with early disease are now also given trastuzumab.

#### Adverse effects

- flu-like symptoms and diarrhoea are common
- cardiotoxicity: more common when anthracyclines have also been used. An echo is usually performed before starting treatment

**Question 47 of 265**

Next

A 59-year-old man with a known history of type 2 diabetes mellitus, atrial fibrillation and epilepsy presents as he is feeling generally unwell. His main complaint is a blue tinge to his vision. Which one of his medications is most likely to be responsible?

<input type="radio"/>	A. Phenytoin
<input type="radio"/>	B. Metformin
<input type="radio"/>	C. Sildenafil
<input type="radio"/>	D. Pioglitazone
<input type="radio"/>	E. Digoxin

Next question

**Visual changes secondary to drugs**

- blue vision: Viagra ('the blue pill')
- yellow-green vision: digoxin

**Sildenafil**

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

**Contraindications**

- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

**Side-effects**

- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects
- headache

A 78-year-old woman with a history of recurrent ventricular tachycardia has routine blood tests 3 months after starting amiodarone therapy:

TSH	14.5 mu/l
Free T4	8.2 pmol/l

How should her thyroid dysfunction be managed?

- ☐ A. Continue amiodarone and add folic acid
- ☐ B. Stop amiodarone and start thyroxine
- ☐ C. Stop amiodarone and add carbimazole and thyroxine
- ☐ D. Stop amiodarone and repeat bloods in 4 weeks
- ☐ E. Continue amiodarone and add thyroxine

Patients who develop hypothyroidism whilst taking amiodarone can continue to take the drug if this is desirable. Given that this patient has a history of ventricular tachycardia it would be unwise to withdraw amiodarone abruptly

### Amiodarone and the thyroid gland

Around 1 in 6 patients taking amiodarone develop thyroid dysfunction

#### Amiodarone-induced hypothyroidism

The pathophysiology of amiodarone-induced hypothyroidism (AIH) is thought to be due to the high iodine content of amiodarone causing a Wolff-Chaikoff effect\*

Amiodarone may be continued if this is desirable

#### Amiodarone-induced thyrotoxicosis

Amiodarone-induced thyrotoxicosis (AIT) may be divided into two types:

	AIT type 1	AIT type 2
Pathophysiology	Excess iodine-induced thyroid hormone synthesis	Amiodarone-related destructive thyroiditis
Goitre	Present	Absent
Management	Carbimazole or potassium perchlorate	Corticosteroids

Unlike in AIH, amiodarone should be stopped if possible in patients who develop AIT

\*an autoregulatory phenomenon where thyroxine formation is inhibited due to high levels of circulating iodide

Which of the following relating to St John's Wort is false?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Adverse effects in trials is similar to placebo                           |
| <input type="radio"/> | B. May cause serotonin syndrome  |
| <input type="radio"/> | C. Mechanism of action is similar to selective serotonin reuptake inhibitors |
| <input type="radio"/> | D. Causes inhibition of the P450 system                                      |
| <input type="radio"/> | E. Has been shown to be effective in treating mild-moderate depression       |

Next question

St John's Wort is a known inducer of the P450 system

### St John's Wort

#### Overview

- shown to be as effective as tricyclic antidepressants in the treatment of mild-moderate depression
- mechanism: thought to be similar to SSRIs (although noradrenaline uptake inhibition has also been demonstrated)
- NICE advise 'may be of benefit in mild or moderate depression, but its use should not be prescribed or advised because of uncertainty about appropriate doses, variation in the nature of preparations, and potential serious interactions with other drugs'

#### Adverse effects

- profile in trials similar to placebo
- can cause serotonin syndrome
- inducer of P450 system, therefore decreased levels of drugs such as warfarin, ciclosporin. The effectiveness of the combined oral contraceptive pill may also be reduced

Which one of the following drugs is not known to induce the cytochrome p450 enzyme system?

<input type="radio"/>	A. Rifampicin
<input type="radio"/>	B. Isoniazid
<input type="radio"/>	C. Phenobarbitone
<input type="radio"/>	D. Griseofulvin
<input type="radio"/>	E. Carbamazepine

[Next question](#)

Isoniazid is an inhibitor of the P450 system

### P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

**Question 51 of 265**

Next

A 54-year-old man with a history of epilepsy and ischaemic heart disease is seen in clinic with a 3 month history of lethargy. Blood tests are as follows:

Hb	9.6 g/dl
MCV	123 fl
Plt	$134 \times 10^9/l$
WCC	$2.6 \times 10^9/l$

Which one of his medications is most likely to be responsible?

<input type="radio"/>	A. Clopidogrel
<input type="radio"/>	B. Atorvastatin
<input type="radio"/>	C. Carbamazepine
<input type="radio"/>	D. Atenolol
<input type="radio"/>	E. Phenytoin

Next question

Phenytoin may cause a megaloblastic anaemia by altering folate metabolism

**Phenytoin**

Phenytoin is used to in the management of seizures.

Mechanism of action

- sodium channel blocker, decreasing the sodium influx into neurons which in turn decreases excitability

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute

- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic

- common: gingival hyperplasia (secondary to increased expression of platelet derived growth factor, PDGF), hirsutism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)

- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

#### Idiosyncratic

- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture\*
- aplastic anaemia
- drug-induced lupus

#### Teratogenic

- associated with cleft palate and congenital heart disease

\*although not listed in the BNF

A 49-year-old man with a history of bipolar disorder, COPD and hypertension is started on a new anti-hypertensive medication. Two weeks later he is admitted to hospital with lithium toxicity. Which medication is most likely to have precipitated this?

<input type="radio"/>	A. Ramipril
<input type="radio"/>	B. Aminophylline
<input type="radio"/>	C. Atenolol
<input type="radio"/>	D. Amlodipine
<input type="radio"/>	E. Doxazosin

[Next question](#)

### Lithium toxicity

Lithium is mood stabilising drug used most commonly prophylactically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys. Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

#### Features of toxicity

- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

#### Management

- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion



Which of the following may reduce the action of aminophylline in patients?

<input type="radio"/>	A. Ciprofloxacin
<input type="radio"/>	B. Acute ethanol consumption
<input type="radio"/>	C. Omeprazole
<input type="radio"/>	D. Smoking
<input type="radio"/>	E. Erythromycin

Next question

Smoking is known to induce CYP1A2 isoenzyme, reducing the effectiveness of aminophylline

### P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

A 56-year-old female with a history of depression is brought in to the Emergency Department by a concerned neighbour. Beside the patient are empty blister packets of co-codamol 30/500, indicating that she may have taken up to 50 tablets. She is confused with a GCS of 14/15 and is unable to say when she took the tablets. What is the most appropriate initial management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Start N-acetyl cysteine immediately                                       |
| <input type="radio"/> | B. Immediate referral for haemodialysis                                      |
| <input type="radio"/> | C. Give naloxone   |
| <input type="radio"/> | D. Start N-acetyl cysteine 4 hours after presentation if levels are elevated |
| <input type="radio"/> | E. Observe   |

[Next question](#)

She may have consumed 25g of paracetamol which is a life-threatening overdose. N-acetyl cysteine needs to be commenced immediately.

There is no mention in the question of respiratory depression or hypoxia to justify the use of naloxone

### Paracetamol overdose: management

#### Management

The following is based on the current BNF guidance. The National Poisons Information Service/TOXBASE should always be consulted for situations outside of the normal parameters.

Activated charcoal should be given if:

- paracetamol dose is in excess of 150 mg/kg (75 mg/kg if high-risk, see below) or 12 g, whichever is the smaller, and;
- the paracetamol was ingested in the previous hour

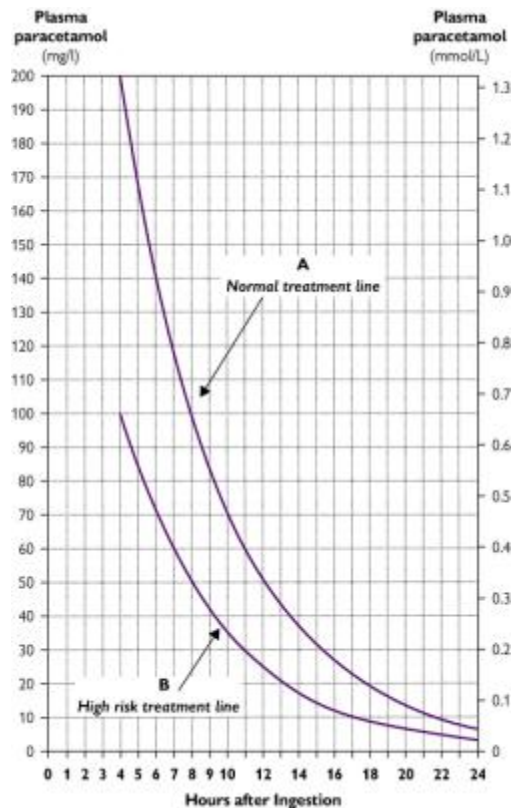
Patients presenting within 8 hours

- paracetamol levels (along with U&Es, LFTs and prothrombin time) should be checked 4 hours after ingestion (earlier samples may be misleading)
- the value should be plotted on a paracetamol treatment graph (see below)
- if the value is above the relevant treatment line intravenous acetylcysteine should be given

Patients presenting 8-24 hours after ingestion

- take an immediate blood sample for paracetamol levels, U&Es, LFTs and prothrombin time

- start acetylcysteine immediately if it is thought that more than 150 mg/kg body weight has been ingested. If the high risk (see below) consider treatment at a lower dose (75 mg/kg)
- otherwise wait for the paracetamol level, give intravenous acetylcysteine if the value is above the relevant treatment line



The following groups of patients are at an increased risk of developing hepatotoxicity following a paracetamol overdose and hence are considered 'high-risk':

- patients taking liver enzyme-inducing drugs (rifampicin, phenytoin, carbamazepine, chronic alcohol excess, St John's Wort)
- malnourished patients (e.g. anorexia or bulimia, cystic fibrosis, hepatitis C, alcoholism, HIV)
- patients who have not eaten for a few days

#### **King's College Hospital criteria for liver transplantation (paracetamol liver failure)**

Arterial pH < 7.3, 24 hours after ingestion

or all of the following:

- prothrombin time > 100 seconds
- creatinine > 300  $\mu\text{mol/L}$
- grade III or IV encephalopathy

A 63-year-old female on long-term warfarin for atrial fibrillation attends the anticoagulation clinic. Despite having a stable INR for the past 4 years on the same dose of warfarin her INR is measured at 5.4. Which one of the following is most likely to be responsible?

<input type="radio"/>	A. St John's Wort
<input type="radio"/>	B. Smoking
<input type="radio"/>	C. Carrot juice
<input type="radio"/>	D. Cranberry juice
<input type="radio"/>	E. Camomile tea

[Next question](#)

St John's Wort is an inducer of the P450 enzyme system so would cause the INR to decrease, rather than increase.

## Warfarin

Warfarin is an oral anticoagulant which inhibits the reduction of vitamin K to its active hydroquinone form, which in turn acts as a cofactor in the formation of clotting factor II, VII, IX and X (mnemonic = 1972) and protein C .

### Indications

- venous thromboembolism: target INR = 2.5, if recurrent 3.5
- atrial fibrillation, target INR = 2.5
- mechanical heart valves, target INR depends on the valve type and location. Mitral valves generally require a higher INR than aortic valves.

Patients on warfarin are monitored using the INR (international normalised ration), the ratio of the prothrombin time for the patient over the normal prothrombin time. Warfarin has a long half-life and achieving a stable INR may take several days. There a variety of loading regimes and computer software is now often used to alter the dose.

### Factors that may potentiate warfarin

- liver disease
- P450 enzyme inhibitors, e.g.: amiodarone, ciprofloxacin
- cranberry juice
- drugs which displace warfarin from plasma albumin, e.g. NSAIDs
- inhibit platelet function: NSAIDs

### Side-effects

- haemorrhage
- teratogenic, although can be used in breast-feeding mothers
- skin necrosis: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis
- purple toes

**Question 56 of 265**

Next

A 46-year-old woman who has recently been diagnosed as having non-Hodgkin's lymphoma is about to start CHOP chemotherapy (cyclophosphamide, hydroxydaunorubicin, vincristine and prednisolone). Her bloods are as follows:

Hb	11.8 g/dl
Platelets	$423 \times 10^9/l$
WBC	$11.2 \times 10^9/l$

Na <sup>+</sup>	143 mmol/l
K <sup>+</sup>	3.9 mmol/l
Urea	6.2 mmol/l
Creatinine	78 µmol/l
Uric acid	0.45 mmol/l

Ciprofloxacin is also prescribed to reduce the risk of neutropenic sepsis. Which other drug should be added to lower the risk of complications?

- ☐ A. Tranexamic acid
- ☐ B. Allopurinol
- ☐ C. Ferrous sulphate
- ☐ D. Aspirin
- ☐ E. Furosemide

Next question

Patients receiving CHOP for non-Hodgkin's lymphoma are at particular risk of tumour lysis syndrome and associated gout secondary to hyperuricaemia. Allopurinol is therefore normally co-prescribed to reduce this risk.

**Allopurinol**

Allopurinol is used in the prevention of gout. It works by inhibiting xanthine oxidase

Initiating allopurinol prophylaxis - see indications below

- allopurinol should not be started until 2 weeks after an acute attack has settled
- initial dose of 100 mg od, with the dose titrated every few weeks to aim for a serum uric acid of < 300 µmol/l
- NSAID or colchicine cover should be used when starting allopurinol

Indications for allopurinol\*

- recurrent attacks - the British Society for Rheumatology recommend 'In uncomplicated gout uric acid lowering drug therapy should be started if a second attack, or further attacks occur within 1 year'
- tophi
- renal disease
- uric acid renal stones
- prophylaxis if on cytotoxics or diuretics

\*patients with Lesch-Nyhan syndrome often take allopurinol for life

## **Interactions**

### Azathioprine

- metabolised to active compound 6-mercaptopurine
- xanthine oxidase is responsible for the oxidation of 6-mercaptopurine to 6-thiouric acid
- allopurinol can therefore lead to high levels of 6-mercaptopurine
- a much reduced dose (e.g. 25%) must therefore be used if the combination cannot be avoided

### Cyclophosphamide

- allopurinol reduces renal clearance, therefore may cause marrow toxicity

Which one of the following may enhance the effects of adenosine?

<input type="radio"/>	A. Diltiazem
<input type="radio"/>	B. Aspirin
<input type="radio"/>	C. Clopidogrel
<input checked="" type="radio"/>	D. Dipyridamole
<input type="radio"/>	E. Aminophylline

Next question

#### Adenosine

- dipyridamole enhances effect
- aminophylline reduces effect

#### Adenosine

The effects of adenosine are enhanced by dipyridamole (anti-platelet agent) and blocked by theophyllines. It should be avoided in asthmatics due to possible bronchospasm.

#### Mechanism of action

- causes transient heart block in the AV node
- agonist of the A1 receptor which inhibits adenylyl cyclase thus reducing cAMP and causing hyperpolarization by increasing outward potassium flux
- adenosine has a very short half-life of about 8-10 seconds

#### Adverse effects

- chest pain
- bronchospasm
- can enhance conduction down accessory pathways, resulting in increased ventricular rate (e.g. WPW syndrome)



Which one of the following statements regarding metformin is false?

<input type="radio"/>	A. Does not cause hypoglycaemia
<input type="radio"/>	B. Increases insulin sensitivity
<input type="radio"/>	C. Decreases hepatic gluconeogenesis
<input type="radio"/>	D. Increases endogenous insulin secretion
<input type="radio"/>	E. Reduces GI absorption of carbohydrates

Sulphonylureas have the property of increasing endogenous insulin secretion

### Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

#### Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

#### Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis\* with severe liver disease or renal failure

#### Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is  $> 130 \mu\text{mol/l}$  and stopping metformin if  $> 150 \mu\text{mol/l}$
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

### Question 59 of 265

A patient is given aspirin 300 mg after developing an acute coronary syndrome. What is the mechanism of action of aspirin to achieve an antiplatelet effect?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Inhibits the production of thromboxane A <sub>2</sub>       |
| <input type="radio"/> | B. Inhibits ADP binding to its platelet receptor               |
| <input type="radio"/> | C. Inhibits the production of prostaglandin H <sub>2</sub>     |
| <input type="radio"/> | D. Glycoprotein IIb/IIIa receptor antagonist                   |
| <input type="radio"/> | E. Inhibits the production of prostacyclin (PGI <sub>2</sub> ) |

[Next question](#)

### Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive

- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

**Antithrombin** treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patient's creatinine is > 265 µmol/l unfractionated heparin should be given.

**Clopidogrel** 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

**Coronary angiography** should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

<b>Aspirin</b>	Antiplatelet - inhibits the production of thromboxane A <sub>2</sub>
<b>Clopidogrel</b>	Antiplatelet - inhibits ADP binding to its platelet receptor
<b>Enoxaparin</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Fondaparinux</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Bivalirudin</b>	Reversible direct thrombin inhibitor

What is the mechanism of action of flecainide?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. Calcium channel blockers    |
| <input type="radio"/> | B. Potassium channel blocker   |
| <input type="radio"/> | C. Sodium channel blocker      |
| <input type="radio"/> | D. Potassium channel activator |
| <input type="radio"/> | E. ADP receptor antagonist     |

Next question

### Flecainide

Flecainide is a Vaughan Williams class 1c antiarrhythmic. It slows conduction of the action potential by acting as a potent sodium channel blocker. This may be reflected by widening of the QRS complex and prolongation of the PR interval

The Cardiac Arrhythmia Suppression Trial (CAST, 1989) investigated the use of agents to treat asymptomatic or mildly symptomatic premature ventricular complexes (PVCs) post myocardial infarction. The hypothesis was that this would reduce deaths from ventricular arrhythmias. Flecainide was actually shown to increase mortality post myocardial infarction and is therefore contraindicated in this situation

#### Indications

- atrial fibrillation
- SVT associated with accessory pathway e.g. Wolf-Parkinson-White syndrome

#### Adverse effects

- negatively inotropic
- bradycardia
- proarrhythmic
- oral paraesthesia
- visual disturbances

A 39-year-old patient is taking phenelzine, a monoamine oxidase inhibitor, for the treatment of depression. Which one of the following foods can the patient safely eat?

<input type="radio"/>	A. Bovril
<input type="radio"/>	B. Cheese
<input type="radio"/>	C. Oxo
<input type="radio"/>	D. Eggs
<input type="radio"/>	E. Broad beans

[Next question](#)

## Monoamine oxidase inhibitors

### Overview

- serotonin and noradrenaline are metabolised by monoamine oxidase in the presynaptic cell

### Non-selective monoamine oxidase inhibitors

- e.g. tranylcypromine, phenelzine
- used in the treatment of depression and other psychiatric disorder
- not used frequently due to side-effects

### Adverse effects of non-selective monoamine oxidase inhibitors

- hypertensive reactions with tyramine containing foods e.g. cheese, pickled herring, Bovril, Oxo, Marmite, broad beans
- anticholinergic effects

Which one of the following drugs demonstrates saturation pharmacokinetics?

<input type="radio"/>	A. Enalapril
<input type="radio"/>	B. Bendrofluazide
<input type="radio"/>	C. Atenolol
<input checked="" type="radio"/>	D. Phenytoin
<input type="radio"/>	E. Paracetamol

Next question

Zero-order (saturation) kinetics

- phenytoin
- alcohol

### Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

### First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are needed orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol

- verapamil
- isoprenaline
- testosterone
- hydrocortisone

Questions concerning zero-order kinetics and acetylator status are also common in the exam

### **Zero-order kinetics**

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

### **Acetylator status**

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

A 45-year-old female with a history of epilepsy is reviewed in the neurology clinic. Which one of the following features is most likely to be attributable to sodium valproate therapy?

<input type="radio"/>	A. Clubbing
<input type="radio"/>	B. Weight loss
<input type="radio"/>	C. Hirsutism
<input type="radio"/>	D. Renal impairment
<input type="radio"/>	E. Tremor

[Next question](#)

Alopecia is much more common than hirsutism in patients treated with sodium valproate.

In the BNF tremor is listed as a 'less frequent' side effect whereas hirsutism is listed as a 'very rare' side effect.

### Sodium valproate

Sodium valproate is used in the management of epilepsy and is first line therapy for generalised seizures. It works by increasing GABA activity.

#### Adverse effects

- gastrointestinal: nausea
- increased appetite and weight gain
- alopecia: regrowth may be curly
- ataxia
- tremor
- hepatitis
- pancreatitis
- thrombocytopaenia
- teratogenic



Where is the site of action of spironolactone?

<input type="radio"/>	A. Proximal convoluted tubule
<input type="radio"/>	B. Ascending loop of Henle
<input type="radio"/>	C. Descending loop of Henle
<input checked="" type="radio"/>	D. Distal convoluted tubule
<input type="radio"/>	E. Macula densa

Next question

## Spironolactone

Spironolactone is an aldosterone antagonist which acts act in the distal convoluted tubule

### Indications

- ascites: patients with cirrhosis develop a secondary hyperaldosteronism. Relatively large doses such as 100 or 200mg are often used
- heart failure (see RALES study below)
- nephrotic syndrome
- Conn's syndrome

### Adverse effects

- hyperkalaemia
- gynaecomastia

### RALES

- NYHA III + IV, patients already taking ACE inhibitor
- low dose spironolactone reduces all cause mortality

A 25-year-old woman is diagnosed with a urinary tract infection. She has a past history of epilepsy and is currently taking sodium valproate. Which one of the following antibiotics should be avoided if possible

<input type="radio"/>	A. Co-amoxiclav
<input type="radio"/>	B. Nitrofurantoin
<input type="radio"/>	C. Cefixime
<input type="radio"/>	D. Trimethoprim
<input type="radio"/>	E. Ciprofloxacin

[Next question](#)

Whilst many antibiotics can lower the seizure threshold, this effect is seen particularly with quinolones. The BNF advises that quinolones 'should be used with caution in patients with a history of epilepsy, or conditions that predispose to seizures'

### Quinolones

Quinolones are a group of antibiotics which work by inhibiting DNA synthesis and are bactericidal in nature. Examples include:

- ciprofloxacin
- levofloxacin

### Adverse effects

- lower seizure threshold in patients with epilepsy
- tendon damage (including rupture) - the risk is increased in patients also taking steroids

A 22-year-old man complains of hearing problems. You perform an examination of his auditory system including Rinne's and Weber's test:

<b>Rinne's test:</b>	Left ear: bone conduction > air conduction Right ear: air conduction > bone conduction
<b>Weber's test:</b>	Lateralises to the left side

What do these tests imply?

- ☐ A. Normal hearing
- ☐ B. Left conductive deafness
- ☐ C. Right conductive deafness
- ☐ D. Left sensorineural deafness
- ☐ E. Right sensorineural deafness

Next question

### Rinne's and Weber's test

Performing both Rinne's and Weber's test allows differentiation of conductive and sensorineural deafness.

Rinne's test

- tuning fork is placed over the mastoid process until the sound is no longer heard, followed by repositioning just over external acoustic meatus
- air conduction (AC) is normally better than bone conduction (BC)
- if  $BC > AC$  then conductive deafness

Weber's test

- tuning fork is placed in the middle of the forehead equidistant from the patient's ears
- the patient is then asked which side is loudest
- in unilateral sensorineural deafness, sound is localised to the unaffected side
- in unilateral conductive deafness, sound is localised to the affected side

Which one of the following pairs of features would be expected to occur following administration of an anticholinesterase (acetylcholinesterase inhibitor)?

<input type="radio"/>	A. Bradycardia and miosis
<input type="radio"/>	B. Bradycardia and urinary retention
<input type="radio"/>	C. Tachycardia and diarrhoea
<input type="radio"/>	D. Bradycardia and mydriasis
<input type="radio"/>	E. Tachycardia and lacrimation

[Next question](#)

A clinical example of an anticholinesterase is organophosphate compounds

### Organophosphate insecticide poisoning

One of the effects of organophosphate poisoning is inhibition of acetylcholinesterase

Features can be predicted by the accumulation of acetylcholine (mnemonic = SLUD)

- Salivation
- Lacrimation
- Urination
- Defecation
- cardiovascular: hypotension, bradycardia
- also: small pupils, muscle fasciculation

### Management

- atropine
- the role of pralidoxime is still unclear - meta-analyses to date have failed to show any clear benefit

What is the mechanism of action of heparin?

- ☐ A. Activates antithrombin III
- ☐ B. Vitamin K antagonist
- ☐ C. Activates tissue plasminogen activator
- ☐ D. Inhibits antithrombin III
- ☐ E. Inhibits protein C

Next question

## Heparin

There are two main types of heparin - unfractionated, 'standard' heparin or low molecular weight heparin (LMWH). Heparins generally act by activating antithrombin III. Unfractionated heparin forms a complex which inhibits thrombin, factors Xa, IXa, XIa and XIIa. LMWH however only increases the action of antithrombin III on factor Xa

The table below shows the differences between standard heparin and LMWH:

	Standard heparin	Low molecular weight heparin (LMWH)
<b>Administration</b>	Intravenous	Subcutaneous
<b>Duration of action</b>	Short	Long
<b>Mechanism of action</b>	Activates antithrombin III. Forms a complex that inhibits thrombin, factors Xa, IXa, XIa and XIIa	Activates antithrombin III. Forms a complex that inhibits factor Xa
<b>Side-effects</b>	Bleeding Heparin-induced thrombocytopenia (HIT) Osteoporosis	Bleeding  Lower risk of HIT and osteoporosis with LMWH
<b>Monitoring</b>	Activated partial thromboplastin time (APTT)	Anti-Factor Xa (although routine monitoring is not required)
<b>Notes</b>	Useful in situations where there is a high risk of bleeding as anticoagulation can be terminated rapidly	Now standard in the management of venous thromboembolism treatment and prophylaxis and acute coronary syndromes

## Heparin-induced thrombocytopenia (HIT)

- immune mediated - antibodies form which cause the activation of platelets
- usually does not develop until after 5-10 days of treatment
- despite being associated with low platelets HIT is actually a prothrombotic condition
- features include a greater than 50% reduction in platelets, thrombosis and skin allergy
- treatment options include alternative anticoagulants such as lepirudin and danaparoid

Both unfractionated and low-molecular weight heparin can cause hyperkalaemia. This is thought to be caused by inhibition of aldosterone secretion.

Heparin overdose may be reversed by protamine sulphate, although this only partially reverses the effect of LMWH.

Which one of the following is least likely to precipitate haemolysis in a patient with G6PD deficiency?

<input type="radio"/>	A. Broad beans
<input type="radio"/>	B. Sepsis
<input type="radio"/>	C. Ciprofloxacin
<input type="radio"/>	D. Primaquine
<input type="radio"/>	E. Penicillin

Next question

### G6PD deficiency

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in a X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

#### Features

- neonatal jaundice is often seen
- intravascular haemolysis
- Heinz bodies on blood films

Diagnosis is made by using a G6PD enzyme assay

#### Some drugs causing haemolysis

- anti-malarials: primaquine
- ciprofloxacin
- sulphonamides

#### Some drugs thought to be safe

- penicillins
- cephalosporins
- macrolides
- tetracyclines
- trimethoprim

A 69-year-old man with terminal lung cancer is reviewed. He currently takes MST 60mg bd for pain. He has become unable to take oral medications and a decision is made to set-up a syringe driver. What dose of diamorphine should be prescribed for the syringe driver?

- |                       |           |
|-----------------------|-----------|
| <input type="radio"/> | A. 60 mg  |
| <input type="radio"/> | B. 40 mg  |
| <input type="radio"/> | C. 120 mg |
| <input type="radio"/> | D. 30 mg  |
| <input type="radio"/> | E. 20 mg  |

[Next question](#)

To convert from oral morphine to diamorphine the total daily morphine dose ( $60 \times 2 = 120\text{mg}$ ) should be divided by 3 ( $120 / 3 = 40\text{mg}$ )

### Palliative care prescribing: pain

#### NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

#### Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered

#### SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred
- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy



## Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

## Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

## Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted. NICE give the following advice on conversion:

- a transdermal fentanyl 12 microgram patch equates to approximately 45 mg oral morphine daily
- a transdermal buprenorphine 20 microgram patch equates to approximately 30 mg oral morphine daily.

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

A patient develops methaemoglobinaemia after being prescribed isosorbide mononitrate. Which substance is most likely to be depleted?

<input type="radio"/>	A. Pyruvate kinase
<input type="radio"/>	B. Hyponitrite reductase
<input type="radio"/>	C. Pyridoxine 5-dehydrogenase
<input type="radio"/>	D. Glucose-6-phosphate dehydrogenase
<input type="radio"/>	E. NADH

[Next question](#)

### Methaemoglobinaemia

Methaemoglobinaemia describes haemoglobin which has been oxidised from  $\text{Fe}^{2+}$  to  $\text{Fe}^{3+}$ . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as  $\text{Fe}^{3+}$  cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

#### Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

#### Acquired causes

- drugs: sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

#### Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal  $\text{pO}_2$  but decreased oxygen saturation

#### Management

- NADH - methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylene blue if acquired

A 35-year-old female diabetic is started on erythromycin for gastroparesis. What is the mechanism of action?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Promotes gastric emptying                  |
| <input type="radio"/> | B. Inhibits bacterial overgrowth              |
| <input type="radio"/> | C. Acts on central chemoreceptor trigger zone |
| <input type="radio"/> | D. Relaxation of pyloric sphincter            |
| <input type="radio"/> | E. Stimulates cholecystokinin release         |

Next question

Erythromycin is used in gastroparesis as it has prokinetic properties

### Macrolides

Erythromycin was the first macrolide used clinically. Newer examples include clarithromycin and azithromycin.

Macrolides act by inhibiting bacterial protein synthesis. If pushed to give an answer they are bacteriostatic in nature, but in reality this depends on the dose and type of organism being treated.

#### Adverse effects

- gastrointestinal side-effects are common. Nausea is less common with clarithromycin than erythromycin
- cholestatic jaundice: risk may be reduced if erythromycin stearate is used
- P450 inhibitor (see below)

#### Common interactions

- statins should be stopped whilst taking a course of macrolides. Macrolides inhibit the cytochrome P450 isoenzyme CYP3A4 that metabolises statins. Taking macrolides concurrently with statins significantly increases the risk of myopathy and rhabdomyolysis.

Which one of the following is least recognised as an adverse effect of taking bendroflumethiazide?

<input type="radio"/>	A. Hypokalaemia
<input type="radio"/>	B. Pseudogout
<input type="radio"/>	C. Hypercalcaemia
<input type="radio"/>	D. Impotence
<input type="radio"/>	E. Impaired glucose tolerance

Next question

Bendroflumethiazide predisposes to gout, rather than pseudogout

### Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide was in the management of hypertension but recent NICE guidelines now recommend other thiazide-like diuretics such as indapamide and chlortalidone.

#### Common adverse effects

- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

#### Rare adverse effects

- thrombocytopaenia
- agranulocytosis
- photosensitivity rash
- pancreatitis

(An eagle eyed user noticed that this entry is very similar to the Wikipedia one. I can assure you that the material has been cut-and-pasted from passmedicine to Wikipedia, and not vice-versa! Note the English spellings of hyponatraemia etc. Check the Wikipedia 'history' page for more details.)

A 34-year-old man with a history of depression is admitted to the Emergency Department. He states he has taken an overdose of both diazepam and dosulepin. On examination blood pressure is 116/78 and the pulse is 140 bpm. His respiratory rate is 8 per minute and the oxygen saturations are 97% on room air. What is the most appropriate next course of action?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Give flumazenil                 |
| <input type="radio"/> | B. Insert a haemodialysis line     |
| <input type="radio"/> | C. Obtain an ECG                   |
| <input type="radio"/> | D. Give naloxone                   |
| <input type="radio"/> | E. Start N-acetylcysteine infusion |

Next question

As this patient has a marked tachycardia the first step would be to obtain an ECG. If changes such as QRS widening are seen then intravenous bicarbonate should be given

Some users have argued that an 'ABC' approach should be taken, with flumazenil given to reverse the respiratory depression. The potential risk of doing this would be inducing a seizure given the coexistent tricyclic overdose

### Tricyclic overdose

Overdose of tricyclic antidepressants is a common presentation to emergency departments. Amitriptyline and dosulepin (dothiepin) are particularly dangerous in overdose.

Early features relate to anticholinergic properties: dry mouth, dilated pupils, agitation, sinus tachycardia, blurred vision.

Features of severe poisoning include:

- arrhythmias
- seizures
- metabolic acidosis
- coma

ECG changes include:

- sinus tachycardia
- widening of QRS
- prolongation of QT interval

Widening of QRS > 100ms is associated with an increased risk of seizures whilst QRS > 160ms is associated

with ventricular arrhythmias

## Management

- IV bicarbonate may reduce the risk of seizures and arrhythmias in severe toxicity
- arrhythmias: class 1a (e.g. Quinidine) and class Ic antiarrhythmics (e.g. Flecainide) are contraindicated as they prolong depolarisation. Class III drugs such as amiodarone should also be avoided as they prolong the QT interval. Response to lignocaine is variable and it should be emphasized that correction of acidosis is the first line in management of tricyclic induced arrhythmias
- dialysis is ineffective in removing tricyclics

What is the mechanism of action of goserelin in prostate cancer?

<input type="radio"/>	A. Androgen receptor antagonist
<input type="radio"/>	B. Oestrogen agonist
<input type="radio"/>	C. GnRH agonist
<input type="radio"/>	D. Luteinising hormone receptor antagonist
<input type="radio"/>	E. GnRH antagonist

Goserelin (Zoladex) is a synthetic GnRH agonist which provides negative feedback to the anterior pituitary

### Prostate cancer: management

#### Localised prostate cancer (T1/T2)

Treatment depends on life expectancy and patient choice. Options include:

- conservative: active monitoring & watchful waiting
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

#### Localised advanced prostate cancer (T3/T4)

Options include:

- hormonal therapy: see below
- radical prostatectomy
- radiotherapy: external beam and brachytherapy

#### Metastatic prostate cancer disease - hormonal therapy

Synthetic GnRH agonist

- e.g. Goserelin (Zoladex)
- cover initially with anti-androgen to prevent rise in testosterone

Anti-androgen

- cyproterone acetate prevents DHT binding from intracytoplasmic protein complexes

Orchidectomy

A 45-year-old man is started on ciclosporin following a renal transplant. Which one of the following adverse effects is most likely to occur?

<input type="radio"/>	A. Depression
<input type="radio"/>	B. Increased risk of ischaemic heart disease
<input type="radio"/>	C. Pulmonary fibrosis
<input type="radio"/>	D. Optic neuritis
<input type="radio"/>	E. Nephrotoxicity

Next question

### Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphatase that activates various transcription factors in T cells

Adverse effects of ciclosporin (note how everything is increased - fluid, BP, K<sup>+</sup>, hair, gums, glucose)

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- gingival hyperplasia
- tremor
- impaired glucose tolerance

Interestingly for an immunosuppressant, ciclosporin is noted by the BNF to be 'virtually non-myelotoxic'.

### Indications

- following organ transplantation
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- ulcerative colitis
- pure red cell aplasia



A 14-year-old girl is taken to the Emergency Department, after being found lying on her bed next to an empty bottle of pills prescribed for her mother. On examination she is agitated, has a clenched jaw and her eyes are deviated upwards. Which drug is she most likely to have consumed?

<input type="radio"/>	A. Phenytoin
<input type="radio"/>	B. Metoclopramide
<input type="radio"/>	C. Amitriptyline
<input type="radio"/>	D. Carbamazepine
<input type="radio"/>	E. Nifedipine

[Next question](#)

This is a classic description of an oculogyric crisis, a form of extrapyramidal disorder

### Oculogyric crisis

An oculogyric crisis is a dystonic reaction to certain drugs or medical conditions

#### Features

- restlessness, agitation
- involuntary upward deviation of the eyes

#### Causes

- phenothiazines
- haloperidol
- metoclopramide
- postencephalitic Parkinson's disease

#### Management

- procyclidine

A 21-year-old student is brought to the Emergency Department by his friends due to him being confused. They report he has been complaining of headaches for the past few weeks. He has a low-grade pyrexia and on examination is noted to have abnormally pink mucosa. What is the most likely diagnosis?

<input type="radio"/>	A. Carbon monoxide poisoning
<input type="radio"/>	B. Meningitis
<input type="radio"/>	C. Paracetamol overdose
<input type="radio"/>	D. Subarachnoid haemorrhage
<input type="radio"/>	E. Methaemoglobinaemia

[Next question](#)

Confusion and pink mucosae are typical features of carbon monoxide poisoning. A low-grade pyrexia is seen in a minority of cases.

### Carbon monoxide poisoning

Carbon monoxide has high affinity for haemoglobin and myoglobin resulting in a left-shift of the oxygen dissociation curve and tissue hypoxia. There are approximately 50 per year deaths from accidental carbon monoxide poisoning in the UK

Questions may hint at badly maintained housing e.g. student houses

Features of carbon monoxide toxicity

- headache: 90% of cases
- nausea and vomiting: 50%
- vertigo: 50%
- confusion: 30%
- subjective weakness: 20%
- severe toxicity: 'pink' skin and mucosae, hyperpyrexia, arrhythmias, extrapyramidal features, coma, death

Typical carboxyhaemoglobin levels

- < 3% non-smokers
- < 10% smokers
- 10 - 30% symptomatic: headache, vomiting
- > 30% severe toxicity

Management

- 100% oxygen

- hyperbaric oxygen

#### Indications for hyperbaric oxygen\*

- loss of consciousness at any point
- neurological signs other than headache
- myocardial ischaemia or arrhythmia
- pregnancy

\*as stated in the 2008 Department of Health publication 'Recognising Carbon Monoxide Poisoning'

A 62-year-old man presents with nocturia, hesitancy and terminal dribbling. Prostate examination reveals a moderately enlarged prostate with no irregular features and a well defined median sulcus. Blood tests show:

PSA	1.3 ng/ml
-----	-----------

What is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Alpha-1 antagonist  |
| <input type="radio"/> | B. 5 alpha-reductase inhibitor                                 |
| <input type="radio"/> | C. Non-urgent referral for transurethral resection of prostate |
| <input type="radio"/> | D. Empirical treatment with ciprofloxacin for 2 weeks          |
| <input type="radio"/> | E. Urgent referral to urology                                  |

Next question

Alpha-1 antagonists are first-line in patients with benign prostatic hyperplasia

### Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition seen in older men.

#### Risk factors

- age: around 50% of 50-year-old men will have evidence of BPH and 30% will have symptoms. Around 80% of 80-year-old men have evidence of BPH
- ethnicity: black > white > Asian

BPH typically presents with lower urinary tract symptoms (LUTS), which may be categorised into:

- voiding symptoms (obstructive): weak or intermittent urinary flow, straining, hesitancy, terminal dribbling and incomplete emptying
- storage symptoms (irritative) urgency, frequency, urgency incontinence and nocturia
- post-micturition: dribbling
- complications: urinary tract infection, retention, obstructive uropathy

#### Management options

- watchful waiting
- medication: alpha-1 antagonists, 5 alpha-reductase inhibitors. The use of combination therapy was supported by the Medical Therapy Of Prostatic Symptoms (MTOPS) trial
- surgery: transurethral resection of prostate (TURP)

Alpha-1 antagonists e.g. tamsulosin, alfuzosin

- decrease smooth muscle tone (prostate and bladder)
- considered first-line, improve symptoms in around 70% of men
- adverse effects: dizziness, postural hypotension, dry mouth, depression

5 alpha-reductase inhibitors e.g. finasteride

- block the conversion of testosterone to dihydrotestosterone (DHT), which is known to induce BPH
- unlike alpha-1 antagonists causes a reduction in prostate volume and hence may slow disease progression. This however takes time and symptoms may not improve for 6 months. They may also decrease PSA concentrations by up to 50%
- adverse effects: erectile dysfunction, reduced libido, ejaculation problems, gynaecomastia

A woman who is 24-weeks pregnant presents with a productive cough. On examination crackles can be heard in the left base and a decision is made to give an antibiotic. Which one of the following is least suitable to prescribe?

<input type="radio"/>	A. Ciprofloxacin
<input type="radio"/>	B. Erythromycin
<input type="radio"/>	C. Co-amoxiclav
<input type="radio"/>	D. Cefalexin
<input type="radio"/>	E. Cefaclor

[Next question](#)

The BNF advises avoiding quinolones in pregnancy due to arthropathy in animal studies

### Prescribing in pregnant patients

Very few drugs are known to be completely safe in pregnancy. The list below largely comprises of those known to be harmful. Some countries have developed a grading system - see the link.

#### Antibiotics

- tetracyclines
- aminoglycosides
- sulphonamides and trimethoprim
- quinolones: the BNF advises to avoid due to arthropathy in some animal studies

#### Other drugs

- ACE inhibitors, angiotensin II receptor antagonists
- statins
- warfarin
- sulfonylureas
- retinoids (including topical)
- cytotoxic agents

The majority of antiepileptics including valproate, carbamazepine and phenytoin are known to be potentially harmful. The decision to stop such treatments however is difficult as uncontrolled epilepsy is also a risk

Which one of the following is least associated with lead poisoning?

<input type="radio"/>	A. Peripheral neuropathy
<input type="radio"/>	B. Acute glomerulonephritis
<input type="radio"/>	C. Blue lines on gum margin
<input type="radio"/>	D. Abdominal pain
<input type="radio"/>	E. Microcytic anaemia

### Lead poisoning

Along with acute intermittent porphyria, lead poisoning should be considered in questions giving a combination of abdominal pain and neurological signs

#### Features

- abdominal pain
- peripheral neuropathy (mainly motor)
- fatigue
- constipation
- blue lines on gum margin (only 20% of adult patients, very rare in children)

#### Investigations

- the blood lead level is usually used for diagnosis. Levels greater than 10 mcg/dl are considered significant
- full blood count: microcytic anaemia. Blood film shows red cell abnormalities including basophilic stippling and clover-leaf morphology
- raised serum and urine levels of delta aminolaevulinic acid may be seen making it sometimes difficult to differentiate from acute intermittent porphyria
- urinary coproporphyrin is also increased (urinary porphobilinogen and uroporphyrin levels are normal to slightly increased)

Management - various chelating agents are currently used:

- dimercaptosuccinic acid (DMSA)
- D-penicillamine
- EDTA
- dimercaprol

What is the most appropriate time to take blood samples for therapeutic monitoring of lithium levels?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. At any time                  |
| <input type="radio"/> | B. Immediately before next dose |
| <input type="radio"/> | C. 4 hours after last dose      |
| <input type="radio"/> | D. 6 hours after last dose      |
| <input type="radio"/> | E. 12 hours after last dose     |

Next question

### Therapeutic drug monitoring

#### Lithium

- range = 0.4 - 1.0 mmol/l
- take 12 hrs post-dose

#### Ciclosporin

- trough levels immediately before dose

#### Digoxin

- at least 6 hrs post-dose

#### Phenytoin

- trough levels immediately before dose



You prescribe sumatriptan to a patient who suffers from migraines. Which one of the following side-effects is most commonly associated with this drug?

<input type="radio"/>	A. Dystonic reactions such as oculogyric crisis
<input type="radio"/>	B. Heartburn
<input type="radio"/>	C. Tightness of the throat and chest
<input type="radio"/>	D. Constipation
<input type="radio"/>	E. Insomnia

[Next question](#)

### **Triptans**

Triptans are specific 5-HT<sub>1</sub> agonists used in the acute treatment of migraine. They are generally used first-line in combination therapy with an NSAID or paracetamol.

#### Prescribing points

- should be taken as soon as possible after the onset of headache, rather than at onset of aura
- oral, orodispersible, nasal spray and subcutaneous injections are available

#### Adverse effects

- 'triptan sensations' - tingling, heat, tightness (e.g. throat and chest), heaviness, pressure

#### Contraindications

- patients with a history of, or significant risk factors for, ischaemic heart disease or cerebrovascular disease

A 79-year-old female with a history of COPD and metastatic lung cancer is admitted with increasing shortness of breath. Following discussion with family it is decided to withdraw active treatment, including fluids and antibiotics, as the admission likely represents a terminal event. Two days after admission she becomes agitated and restless. What is the most appropriate management?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Subcutaneous midazolam            |
| <input type="radio"/> | B. Intramuscular haloperidol         |
| <input type="radio"/> | C. Oral lormetazepam                 |
| <input type="radio"/> | D. Oral haloperidol                  |
| <input type="radio"/> | E. Recommence fluids and antibiotics |

[Next question](#)

### Palliative care prescribing: agitation and confusion

Underlying causes of confusion need to be looked for and treated as appropriate, for example hypercalcaemia, infection, urinary retention and medication. If specific treatments fail then the following may be tried:

- first choice: haloperidol
- other options: chlorpromazine, levomepromazine

In the terminal phase of the illness (for example a patient on the Care of the Dying pathway) then agitation or restlessness is best treated with midazolam

Which one of the following drugs is most likely to cause impaired glucose tolerance?

<input type="radio"/>	A. Sulfasalazine
<input type="radio"/>	B. Azathioprine
<input type="radio"/>	C. Leflunomide
<input type="radio"/>	D. Methotrexate
<input type="radio"/>	E. Tacrolimus

Next question

### Drug-induced impaired glucose tolerance

Drugs which are known to cause impaired glucose tolerance include:

- thiazides, furosemide (less common)
- steroids
- tacrolimus, ciclosporin
- interferon-alpha
- nicotinic acid
- atypical antipsychotics e.g. olanzapine

Beta-blockers cause a slight impairment of glucose tolerance. They should also be used with caution in diabetics as they can interfere with the metabolic and autonomic responses to hypoglycaemia

A 45-year-old man is prescribed bupropion to help him quit smoking. What is the mechanism of action of bupropion?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Nicotinic receptor partial agonist                                       |
| <input type="radio"/> | B. Selective serotonin reuptake inhibitor                                   |
| <input type="radio"/> | C. Norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist |
| <input type="radio"/> | D. Dopamine agonist   |
| <input type="radio"/> | E. Dopamine antagonist  |

[Next question](#)

## Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

### Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

### Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop
- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)

- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

## Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication

Which one of the following patients should not automatically be prescribed a statin in the absence of any contraindication?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. A 51-year-old man who had a myocardial infarction 4 years ago and is now asymptomatic |
| <input type="radio"/> | B. A 57-year-old female smoker with a 10-year cardiovascular risk of 23%                 |
| <input type="radio"/> | C. A 53-year-old man with intermittent claudication                                      |
| <input type="radio"/> | D. A 62-year-old man who had a transient ischaemic attack 10 months ago                  |
| <input type="radio"/> | E. A 37-year-old man with well controlled diabetes mellitus type 2                       |

Next question

## Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

### Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

### Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk  $\geq 20\%$
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering\*

	Total cholesterol (mmol/l)	LDL cholesterol
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

\*current NICE guidelines do not recommend a target cholesterol in primary prevention

A 24-year-old with a history of Crohn's disease is started on azathioprine. What is the mechanism of action of azathioprine?

<input type="radio"/>	A. Inhibits purine synthesis
<input type="radio"/>	B. Inhibits inosine monophosphate dehydrogenase
<input type="radio"/>	C. Mercaptopurine antagonist
<input type="radio"/>	D. Thiopurine methyltransferase inhibitor
<input type="radio"/>	E. Causes cross-linking in DNA

[Next question](#)

### Azathioprine

Azathioprine is metabolised to the active compound mercaptopurine, a purine analogue that inhibits purine synthesis. A thiopurine methyltransferase (TPMT) test may be needed to look for individuals prone to azathioprine toxicity.

Adverse effects include

- bone marrow depression
- nausea/vomiting
- pancreatitis

A significant interaction may occur with allopurinol and hence lower doses of azathioprine should be used.



A 52-year-old man with a history of epilepsy is reviewed. Since having his medication change he has experienced a 'numbness' of his hands and feet. On examination he has reduced sensation in a glove-and-stocking distribution associated with a reduced ankle reflex. He is also noted to have lymphadenopathy in the cervical and inguinal region and some bleeding around the gums. Which one of the following medications is he most likely to have been taking?

<input type="radio"/>	A. Carbamazepine
<input type="radio"/>	B. Phenytoin
<input type="radio"/>	C. Topiramate
<input type="radio"/>	D. Sodium valproate
<input type="radio"/>	E. Lamotrigine

[Next question](#)

## Phenytoin

Phenytoin is used to in the management of seizures.

Mechanism of action

- sodium channel blocker, decreasing the sodium influx into neurons which in turn decreases excitability

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute

- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic

- common: gingival hyperplasia (secondary to increased expression of platelet derived growth factor, PDGF), hirsutism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

## Idiosyncratic

- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture\*
- aplastic anaemia
- drug-induced lupus

## Teratogenic

- associated with cleft palate and congenital heart disease

\*although not listed in the BNF

What is the mechanism of action of exenatide?

<input type="radio"/>	A. Glucagon inhibitor
<input type="radio"/>	B. Dipeptidyl peptidase-4 (DPP-4) inhibitor
<input type="radio"/>	C. Glucagon-like peptide-1 (GLP-1) mimetic
<input type="radio"/>	D. Incretin inhibitor
<input type="radio"/>	E. Alpha-glucosidase inhibitor

Next question

Exenatide = Glucagon-like peptide-1 (GLP-1) mimetic

### Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HbA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

A patient with poorly controlled asthma is started on montelukast. What is the mechanism of action of this drug?

- ☐ A. Beta-2 receptor antagonist
- ☐ B. Beta-2 receptor agonist
- ☐ C. Leukotriene receptor agonist
- ☐ D. Leukotriene receptor antagonist
- ☐ E. Phosphodiesterase type-4 inhibitor

[Next question](#)

### Asthma: stepwise management in adults

The management of stable asthma is now well established with a step-wise approach:

<b>Step 1</b>	Inhaled short-acting B2 agonist as required
<b>Step 2</b>	Add inhaled steroid at 200-800 mcg/day*  400 mcg is an appropriate starting dose for many patients. Start at dose of inhaled steroid appropriate to severity of disease
<b>Step 3</b>	1. Add inhaled long-acting B2 agonist (LABA)  2. Assess control of asthma: <ul style="list-style-type: none"> <li>• good response to LABA - continue LABA</li> <li>• benefit from LABA but control still inadequate: continue LABA and increase inhaled steroid dose to 800 mcg/day* (if not already on this dose)</li> <li>• no response to LABA: stop LABA and increase inhaled steroid to 800 mcg/ day.* If control still inadequate, institute trial of other therapies, leukotriene receptor antagonist or SR theophylline</li> </ul>
<b>Step 4</b>	Consider trials of: <ul style="list-style-type: none"> <li>• increasing inhaled steroid up to 2000 mcg/day*</li> <li>• addition of a fourth drug e.g. Leukotriene receptor antagonist, SR theophylline, B2 agonist tablet</li> </ul>
<b>Step 5</b>	Use daily steroid tablet in lowest dose providing adequate control. Consider other treatments to minimise the use of steroid tablets

	Maintain high dose inhaled steroid at 2000 mcg/day*
	Refer patient for specialist care

\*beclometasone dipropionate or equivalent

### **Additional notes**

Leukotriene receptor antagonists

- e.g. Montelukast, zafirlukast
- have both anti-inflammatory and bronchodilatory properties
- should be used when patients are poorly controlled on high-dose inhaled corticosteroids and a long-acting b2-agonist
- particularly useful in aspirin-induced asthma
- associated with the development of Churg-Strauss syndrome

Fluticasone is more lipophilic and has a longer duration of action than beclometasone

Hydrofluoroalkane is now replacing chlorofluorocarbon as the propellant of choice. Only half the usually dose is needed with hydrofluoroalkane due to the smaller size of the particles

Long acting B2-agonists acts as bronchodilators but also inhibit mediator release from mast cells. Recent meta-analysis showed adding salmeterol improved symptoms compared to doubling the inhaled steroid dose

What is the main mechanism of action of ondansetron?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Dopamine receptor agonist             |
| <input type="radio"/> | B. 5-HT <sub>2</sub> receptor antagonist |
| <input type="radio"/> | C. Dopamine receptor antagonist          |
| <input type="radio"/> | D. 5-HT <sub>2</sub> receptor agonist    |
| <input type="radio"/> | E. 5-HT <sub>3</sub> receptor antagonist |

Next question

### Drugs which act on serotonin receptors

Below is a summary of drugs which are known to act via modulation of the serotonin (5-HT) system. It should be noted that 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis

#### Agonists

- sumatriptan is a 5-HT<sub>1D</sub> receptor agonist which is used in the acute treatment of migraine
- ergotamine is a partial agonist of 5-HT<sub>1</sub> receptors

#### Antagonists

- pizotifen is a 5-HT<sub>2</sub> receptor antagonist used in the prophylaxis of migraine attacks. Methysergide is another antagonist of the 5-HT<sub>2</sub> receptor but is rarely used due to the risk of retroperitoneal fibrosis
- cyproheptadine is a 5-HT<sub>2</sub> receptor antagonist which is used to control diarrhoea in patients with carcinoid syndrome
- ondansetron is a 5-HT<sub>3</sub> receptor antagonist and is used as an antiemetic

**Question 93 of 265**

Next

A 14-year-old boy is brought to the Emergency Department. Whilst in school he injected his friends EpiPen into the palm of his left hand. Shortly afterwards the left middle finger became cold and pale. The capillary refill time was around 5-6 seconds. What is the most appropriate management?

<input type="radio"/>	A. Inhalation of Nitrox (mixture of nitrogen + oxygen)
<input type="radio"/>	B. Intravenous nitrate infusion
<input type="radio"/>	C. Local infiltration of histamine
<input type="radio"/>	D. Intravenous prostacyclin infusion
<input type="radio"/>	E. Local infiltration of phentolamine

Next question

Adrenaline induced ischaemia - phentolamine

Phentolamine, a short acting alpha blocker, may be used in this situation. It is normally used mainly to control blood pressure during surgical resection of pheochromocytoma

**Adrenaline**

Adrenaline is a sympathomimetic amine with both alpha and beta adrenergic stimulating properties

**Indications**

- anaphylaxis
- cardiac arrest

**Recommend Adult Life Support (ALS) adrenaline doses**

- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

**Management of accidental injection**

- local infiltration of phentolamine



**Question 94 of 265**

Next

A 67-year-old woman is noted to have corneal opacities during a routine opticians appointment. These are not affecting her vision. Which one of the following drugs is most likely to be the cause?

<input type="radio"/>	A. Amiodarone
<input type="radio"/>	B. Sodium valproate
<input type="radio"/>	C. Methotrexate
<input type="radio"/>	D. Frusemide
<input type="radio"/>	E. Digoxin

Next question

Amiodarone therapy can result in both corneal opacities and optic neuritis

**Drugs causing ocular problems**

## Cataracts

- steroids

## Corneal opacities

- amiodarone
- indomethacin

## Optic neuritis

- ethambutol
- amiodarone
- metronidazole

## Retinopathy

- chloroquine, quinine

Sildenafil can cause both blue discolouration and non-arteritic anterior ischaemic neuropathy

A 72-year-old man with metastatic colon cancer is reviewed. He currently takes co-codamol 30/500 2 tablets qds for pain relief. Unfortunately this is not controlling his pain. What is the most appropriate change to his medication?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Switch to MST 15mg bd + paracetamol 1g qds |
| <input type="radio"/> | B. Switch to MST 35mg bd + paracetamol 1g qds |
| <input type="radio"/> | C. Add tramadol 50-100mg 1-2 qds              |
| <input type="radio"/> | D. Switch to MST 25mg bd                      |
| <input type="radio"/> | E. Switch to MST 15mg bd                      |

Next question

His total codeine dose is  $30 * 2 * 4 = 240$  mg/day. Converting this to oral morphine = 24 mg/day. It is therefore reasonable to start MST 15mg bd as his pain is not currently controlled. Paracetamol should be continued as it has been shown to give benefits even to patients on large doses of morphine

### Palliative care prescribing: pain

#### NICE guidelines

In 2012 NICE published guidelines on the use of opioids in palliative care. Selected points are listed below. Please see the link for more details.

#### Starting treatment

- when starting treatment, offer patients with advanced and progressive disease regular oral modified-release (MR) or oral immediate-release morphine (depending on patient preference), with oral immediate-release morphine for breakthrough pain
- if no comorbidities use 20-30mg of MR a day with 5mg morphine for breakthrough pain. For example, 15mg modified-release morphine tablets twice a day with 5mg of oral morphine solution as required
- oral modified-release morphine should be used in preference to transdermal patches
- laxatives should be prescribed for all patients initiating strong opioids
- patients should be advised that nausea is often transient. If it persists then an antiemetic should be offered

#### SIGN guidelines

SIGN issued guidance on the control of pain in adults with cancer in 2008. Selected points

- the breakthrough dose of morphine is one-sixth the daily dose of morphine
- all patients who receive opioids should be prescribed a laxative
- opioids should be used with caution in patients with chronic kidney disease. Alfentanil, buprenorphine and fentanyl are preferred

- metastatic bone pain may respond to NSAIDs, bisphosphonates or radiotherapy

## Other points

When increasing the dose of opioids the next dose should be increased by 30-50%.

## Opioid side-effects

Usually transient	Usually persistent
Nausea Drowsiness	Constipation

## Conversion between opioids

From	To	
Oral codeine	Oral morphine	Divide by 10
Oral tramadol	Oral morphine	Divide by 5

From	To	
Oral morphine	Oral oxycodone	Divide by 2

The BNF states that oral morphine sulphate 80-90mg over 24 hours is approximately equivalent to one '25 mcg/hour' fentanyl patch, therefore product literature should be consulted. NICE give the following advice on conversion:

- a transdermal fentanyl 12 microgram patch equates to approximately 45 mg oral morphine daily
- a transdermal buprenorphine 20 microgram patch equates to approximately 30 mg oral morphine daily.

From	To	
Oral morphine	Subcutaneous diamorphine	Divide by 3
Oral oxycodone	Subcutaneous diamorphine	Divide by 1.5

A 43-year-old man with a history of bipolar disorder is admitted with acute confusion. Whilst being transferred to hospital he had generalised seizure which terminated spontaneously after around 30 seconds. On arrival in the Emergency Department his GCS is 14/15 and he is noted to have a coarse tremor. A diagnosis of lithium toxicity is suspected. Intravenous access is obtained, bloods are taken and a saline infusion is started. Blood results reveal the following:

Lithium level	4.2 mmol/l
Na <sup>+</sup>	136 mmol/l
K <sup>+</sup>	4.6 mmol/l
Urea	8.1 mmol/l
Creatinine	99 µmol/l
Bicarbonate	18 mmol/l

What is the most appropriate management?

- ☐ A. Arrange haemodialysis
- ☐ B. Intravenous magnesium
- ☐ C. Intravenous bicarbonate
- ☐ D. Intravenous hypertonic saline
- ☐ E. Arrange plasma exchange

Next question

The high lithium level and reduced GCS are an indication for haemodialysis in this patient.

### Lithium toxicity

Lithium is mood stabilising drug used most commonly prophylactically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys. Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

Features of toxicity

- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

## Management

- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

A 34-year-old female with a history of anti-phospholipid syndrome is reviewed in clinic. She is on long-term warfarin and her INR has been stable at 3.0 for over 2 years. Measurement from one week ago and today shows values of 1.5 and 1.3 respectively. Which one of the following medications is most likely to be responsible?

<input type="radio"/>	A. Ciprofloxacin
<input type="radio"/>	B. Fluconazole
<input type="radio"/>	C. Sodium valproate
<input type="radio"/>	D. Carbamazepine
<input type="radio"/>	E. Cimetidine

[Next question](#)

Carbamazepine is an enzyme inducer, the other listed medications are inhibitors

### P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

What is the mechanism of action of aminophylline?

<input type="radio"/>	A. Leukotriene receptor antagonists
<input type="radio"/>	B. Beta 2-adrenoceptor agonist
<input type="radio"/>	C. Muscarinic receptor antagonist
<input type="radio"/>	D. Phosphodiesterase inhibitor
<input type="radio"/>	E. Beta 2-adrenoceptor antagonist

Next question

This is a rather unfair question as the mechanism of action of theophyllines has yet to be fully unravelled

### Theophylline

Theophylline, like caffeine, is one of the naturally occurring methylxanthines. The main use of theophyllines in clinical medicine is as a bronchodilator in the management of asthma and COPD

The exact mechanism of action has yet to be discovered. One theory suggests theophyllines may be a non-specific inhibitor of phosphodiesterase resulting in an increase in cAMP. Other proposed mechanisms include antagonism of adenosine and prostaglandin inhibition

### Theophylline poisoning

#### Features

- acidosis, hypokalaemia
- vomiting
- tachycardia, arrhythmias
- seizures

#### Management

- activated charcoal
- charcoal haemoperfusion is preferable to haemodialysis

A patient with glucose-6-phosphate dehydrogenase (G6PD) deficiency presents for advice about malaria prophylaxis. He is about to go on a 'gap year' during which he will be travelling abroad for 12 months. Which one of the following medications is it most important that he avoids?

<input type="radio"/>	A. Artemether with lumefantrine
<input type="radio"/>	B. Mefloquine
<input type="radio"/>	C. Proguanil
<input type="radio"/>	D. Doxycycline
<input type="radio"/>	E. Primaquine

[Next question](#)

### G6PD deficiency

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in a X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

#### Features

- neonatal jaundice is often seen
- intravascular haemolysis
- Heinz bodies on blood films

Diagnosis is made by using a G6PD enzyme assay

#### Some drugs causing haemolysis

- anti-malarials: primaquine
- ciprofloxacin
- sulphonamides

#### Some drugs thought to be safe

- penicillins
- cephalosporins
- macrolides
- tetracyclines
- trimethoprim



A 57-year-old man with a history of ischaemic heart disease is keen to try sildenafil for erectile dysfunction. Which one of the following medications may contraindicate its use?

<input type="radio"/>	A. Nebivolol
<input type="radio"/>	B. Losartan
<input type="radio"/>	C. Nicorandil
<input type="radio"/>	D. Nifedipine
<input type="radio"/>	E. Ramipril

[Next question](#)

Viagra? - contraindicated by nitrates and nicorandil

Nicorandil has a nitrate component as well as being a potassium channel activator

### Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

#### Contraindications

- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

#### Side-effects

- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects
- headache

Which one of the following drugs used in the management of diabetes mellitus is most likely to cause cholestasis?

<input type="radio"/>	A. Metformin
<input type="radio"/>	B. Gliclazide
<input type="radio"/>	C. Acarbose
<input type="radio"/>	D. Rosiglitazone
<input type="radio"/>	E. Insulin

### Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin\*, nitrofurantoin
- anabolic steroids, testosterone
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

\*risk may be reduced with erythromycin stearate

An 80-year-old woman is started on oral alendronate following a fractured neck of femur. How would you explain how to take the tablet?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Take it on a full stomach to minimise gastric irritation and avoid lying down for 30 minutes afterwards |
| <input type="radio"/> | B. Dissolve tablet in water and take just before breakfast + sit-upright for 30 minutes following          |
| <input type="radio"/> | C. Take during main evening meal + sit-upright for 2 hours following                                       |
| <input type="radio"/> | D. Take at least 30 minutes before breakfast with plenty of water + sit-upright for 30 minutes following   |
| <input type="radio"/> | E. Take at least 30 minutes after a main meal + sit-upright for 30 minutes following                       |

[Next question](#)

Bisphosphonates can cause a variety of oesophageal problems

## Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

### Clinical uses

- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metastases

### Adverse effects

- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw
- increased risk of atypical stress fractures of the proximal femoral shaft in patients taking alendronate

The BNF suggests the following counselling for patients taking oral bisphosphonates

- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

The INR of a patient who has recently started treatment for tuberculosis drops from 2.6 to 1.3. Which one of the following medications is most likely to be responsible?

<input type="radio"/>	A. Rifampicin
<input type="radio"/>	B. Streptomycin
<input type="radio"/>	C. Ethambutol
<input type="radio"/>	D. Isoniazid
<input type="radio"/>	E. Pyrazinamide

[Next question](#)

Rifampicin is a P450 enzyme inducer and will therefore increase the metabolism of warfarin, therefore decreasing the INR.

### P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

Which one of the following statements regarding quinupristin is incorrect?

<input type="radio"/>	A. Thrombophlebitis is a recognised side-effect
<input type="radio"/>	B. Has broad Gram positive cover
<input type="radio"/>	C. Inhibits bacterial protein synthesis
<input type="radio"/>	D. Acts as a P450 inhibitor
<input type="radio"/>	E. Particularly useful against <i>Enterococcus faecalis</i>

Next question

### Quinupristin & dalfopristin antibiotics

#### Overview

- injectable streptogramin antibiotic
- combination of group A and group B streptogramin
- inhibits bacterial protein synthesis by blocking tRNA complexes binding to the ribosome

#### Spectrum

- most Gram positive bacteria
- exception: *Enterococcus faecalis*\*

#### Adverse effects

- thrombophlebitis (give via a central line)
- arthralgia
- P450 inhibitor

\*not to be confused with *Enterococcus faecium*, which is sensitive to Quinupristin & dalfopristin

A patient with testicular cancer is started on cisplatin therapy. Which of the following side-effects is most characteristically associated with cisplatin?

- ☐ A. Liver cirrhosis
- ☐ B. Alopecia
- ☐ C. Peripheral neuropathy
- ☐ D. Haemorrhagic cystitis
- ☐ E. Cardiomyopathy

Next question

### Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

What is the most appropriate time to take blood samples for therapeutic monitoring of ciclosporin levels?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. 6 hours after last dose      |
| <input type="radio"/> | B. Immediately before next dose |
| <input type="radio"/> | C. At any time                  |
| <input type="radio"/> | D. 12 hours after last dose     |
| <input type="radio"/> | E. 4 hours after last dose      |

Next question

### Therapeutic drug monitoring

#### Lithium

- range = 0.4 - 1.0 mmol/l
- take 12 hrs post-dose

#### Ciclosporin

- trough levels immediately before dose

#### Digoxin

- at least 6 hrs post-dose

#### Phenytoin

- trough levels immediately before dose

In the Vaughan Williams classification of antiarrhythmics lidocaine is an example of a:

- ☐ A. Class Ia agent
- ☐ B. Class Ib agent
- ☐ C. Class Ic agent
- ☐ D. Class II agent
- ☐ E. Class IV agent

Next question

### Antiarrhythmics: Vaughan Williams classification

The Vaughan Williams classification of antiarrhythmics is still widely used although it should be noted that a number of common drugs are not included in the classification e.g. adenosine, atropine, digoxin and magnesium

Class	Example	Mechanism of action
Ia	Disopyramide	Block sodium channels
Ib	Lidocaine	Block sodium channels
Ic	Flecainide	Block sodium channels
II	Propranolol	Beta-adrenoceptor antagonists
III	Amiodarone	Block potassium channels
IV	Verapamil	Calcium channel blockers



In line with NICE guidelines on the secondary prevention of osteoporotic fractures in postmenopausal women, which one of the following patients should not automatically be started on treatment?

<input type="radio"/>	A. A 81-year-old woman who has had a fractured neck of femur
<input type="radio"/>	B. A 64-year-old women with a wedge fractures of her thoracic spine. DEXA scan shows a T-score of -3.1 SD
<input type="radio"/>	C. A 55-year-old women who had a Colles fracture of the wrist. DEXA scan shows a T-score of -3.3 SD
<input type="radio"/>	D. A 64-year-old women with a BMI of 18 kg/m <sup>2</sup> . She has a wedge fractures of her thoracic spine. DEXA scan shows a T-score of -2.7 SD
<input type="radio"/>	E. A 71-year-old women who had a Colles fracture of the wrist. DEXA scan shows a T-score of -2.1 SD

Next question

### Osteoporosis: secondary prevention

NICE guidelines were updated in 2008 on the secondary prevention of osteoporotic fractures in postmenopausal women.

Key points include

- treatment is indicated following osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (a T-score of - 2.5 SD or below). In women aged 75 years or older, a DEXA scan may not be required 'if the responsible clinician considers it to be clinically inappropriate or unfeasible'
- vitamin D and calcium supplementation should be offered to all women unless the clinician is confident they have adequate calcium intake and are vitamin D replete
- alendronate is first-line
- around 25% of patients cannot tolerate alendronate, usually due to upper gastrointestinal problems. These patients should be offered risendronate or etidronate (see treatment criteria below)
- strontium ranelate and raloxifene are recommended if patients cannot tolerate bisphosphonates (see treatment criteria below)

### Treatment criteria for patients not taking alendronate

Unfortunately, a number of complicated treatment cut-off tables have been produced in the latest guidelines for patients who do not tolerate alendronate

Risk factors (for use in the tables below)

- parental history of hip fracture

- alcohol intake of 4 or more units per day
- rheumatoid arthritis

T-scores (SD) at (or below) which risedronate or etidronate is recommended when alendronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50-54	Not indicated	- 3.0	- 2.5
55-59	- 3.0	- 3.0	- 2.5
60-64	- 3.0	- 3.0	- 2.5
65-69	- 3.0	- 2.5	- 2.5
70 or older	- 2.5	- 2.5	- 2.5

T-scores (SD) at (or below) which strontium ranelate or raloxifene is recommended when alendronate and either risedronate or etidronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50-54	Not indicated	- 3.5	- 3.5
55-59	- 4.0	- 3.5	- 3.5
60-64	- 4.0	- 3.5	- 3.5
65-69	- 4.0	- 3.5	- 3.0
70-74	- 3.0	- 3.0	- 2.5
75 or older	- 3.0	- 2.5	- 2.5

## Supplementary notes on treatment

### Bisphosphonates

- alendronate, risedronate and etidronate are all licensed for the prevention and treatment of post-menopausal and glucocorticoid-induced osteoporosis
- all three have been shown to reduce the risk of both vertebral and non-vertebral fractures although alendronate, risedronate may be superior to etidronate in preventing hip fractures
- ibandronate is a once-monthly oral bisphosphonate

### Vitamin D and calcium

- poor evidence base to suggest reduced fracture rates in the general population at risk of osteoporotic fractures - may reduce rates in frail, housebound patients

#### Raloxifene - selective oestrogen receptor modulator (SERM)

- has been shown to prevent bone loss and to reduce the risk of vertebral fractures, but has not yet been shown to reduce the risk of non-vertebral fractures
- has been shown to increase bone density in the spine and proximal femur
- may worsen menopausal symptoms
- increased risk of thromboembolic events
- may decrease risk of breast cancer

#### Strontium ranelate

- 'dual action bone agent' - increases deposition of new bone by osteoblasts and reduces the resorption of bone by osteoclasts
- strong evidence base, may be second-line treatment in near future
- increased risk of thromboembolic events

#### Teriparatide

- recombinant form of parathyroid hormone
- very effective at increasing bone mineral density but role in the management of osteoporosis yet to be clearly defined

#### Hormone replacement therapy

- has been shown to reduce the incidence of vertebral fracture and non-vertebral fractures
- due to concerns about increased rates of cardiovascular disease and breast cancer it is no longer recommended for primary or secondary prevention of osteoporosis unless the woman is suffering from vasomotor symptoms

#### Hip protectors

- evidence to suggest significantly reduce hip fractures in nursing home patients
- compliance is a problem

#### Falls risk assessment

- no evidence to suggest reduced fracture rates
- however, do reduce rate of falls and should be considered in management of high risk patients

A 71-year-old man who has atrial fibrillation and heart failure is started on digoxin. What is the mechanism of action of digoxin?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Blocks $\text{Ca}^{2+}$ release from the sarcoplasmic reticulum |
| <input type="radio"/> | B. Blocks $\text{Na}^{+}$ entry into myocytes                      |
| <input type="radio"/> | C. Agonist of the myocyte sodium-calcium exchanger                 |
| <input type="radio"/> | D. $\text{K}^{+}$ channel blocker                                  |
| <input type="radio"/> | E. Inhibits the $\text{Na}^{+}/\text{K}^{+}$ ATPase pump           |

[Next question](#)

Digoxin - inhibits the  $\text{Na}^{+}/\text{K}^{+}$  ATPase pump

### Digoxin and digoxin toxicity

Digoxin is a cardiac glycoside now mainly used for rate control in the management of atrial fibrillation. As it has positive inotropic properties it is sometimes used for improving symptoms (but not mortality) in patients with heart failure.

Mechanism of action

- decreases conduction through the atrioventricular node which slows the ventricular rate in atrial fibrillation and flutter
- increases the force of cardiac muscle contraction due to inhibition of the  $\text{Na}^{+}/\text{K}^{+}$  ATPase pump

### Digoxin toxicity

Plasma concentration alone does not determine whether a patient has developed digoxin toxicity. The BNF advises that the likelihood of toxicity increases progressively from 1.5 to 3 mcg/l.

Features

- generally unwell, lethargy, nausea & vomiting, anorexia, confusion, yellow-green vision
- arrhythmias (e.g. AV block, bradycardia)

Precipitating factors

- classically: hypokalaemia\*

- increasing age
- renal failure
- myocardial ischaemia
- hypomagnesaemia, hypercalcaemia, hypernatraemia, acidosis
- hypoalbuminaemia
- hypothermia
- hypothyroidism
- drugs: amiodarone, quinidine, verapamil, diltiazem, spironolactone (compete for secretion in distal convoluted tubule therefore reduce excretion). Also drugs which cause hypokalaemia e.g. thiazides and loop diuretics

## Management

- Digibind
- correct arrhythmias
- monitor potassium

\*hyperkalaemia may also worsen digoxin toxicity, although this is very small print

You receive the blood results of a 76-year-old man who takes warfarin following a pulmonary embolism two months ago. He recently completed a course of antibiotics.

INR	8.4
-----	-----

On reviewing the patient he is well with no bleeding or bruising. What is the most appropriate action?

- ☐ A. Stop warfarin + restart when INR < 5.0 + give low-molecular weight heparin until warfarin restarted
- ☐ B. Oral vitamin K 5mg + stop warfarin + repeat INR after 24 hours
- ☐ C. Stop warfarin + restart when INR < 3.0
- ☐ D. Stop warfarin + restart when INR < 5.0
- ☐ E. Fresh frozen plasma + restart warfarin when INR < 5.0

The BNF recommends a dose of between 1 to 5mg of vitamin K in this situation.

### Warfarin overdose

The following is based on the BNF guidelines, which in turn take into account the British Committee for Standards in Haematology (BCSH) guidelines. A 2005 update of the BCSH guidelines emphasised the preference of prothrombin complex concentrate over FFP in major bleeding.

<b>Major bleeding</b>	Stop warfarin Give intravenous vitamin K 5mg Prothrombin complex concentrate - if not available then FFP*
<b>INR &gt; 8.0</b> <b>Minor bleeding</b>	Stop warfarin Give intravenous vitamin K 1-3mg Repeat dose of vitamin K if INR still too high after 24 hours Restart warfarin when INR < 5.0
<b>INR &gt; 8.0</b> <b>No bleeding</b>	Stop warfarin Give oral vitamin K 1-5mg Repeat dose of vitamin K if INR still too high after 24 hours Restart when INR < 5.0
<b>INR 5.0-8.0</b> <b>Minor bleeding</b>	Stop warfarin Give intravenous vitamin K 1-3mg Restart when INR < 5.0
<b>INR 5.0-8.0</b> <b>No bleeding</b>	Withhold 1 or 2 doses of warfarin Reduce subsequent maintenance dose

\*as FFP can take time to defrost prothrombin complex concentrate should be considered in cases of intracranial haemorrhage

A 72-year-old man is reviewed in the diabetes clinic. He has a history of heart failure and type 2 diabetes mellitus. His current medications include furosemide 40mg od, ramipril 10mg od and bisoprolol 5mg od. Clinical examination is unremarkable with no evidence of peripheral oedema, a clear chest and blood pressure of 130/76 mmHg. Recent renal and liver function tests are normal. Which one of the following medications is contraindicated?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Sitagliptin  |
| <input type="radio"/> | B. Pioglitazone |
| <input type="radio"/> | C. Gliclazide   |
| <input type="radio"/> | D. Exenatide    |
| <input type="radio"/> | E. Metformin    |

[Next question](#)

Thiazolidinediones are absolutely contraindicated in heart failure

### Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance. Rosiglitazone was withdrawn in 2010 following concerns about the cardiovascular side-effect profile.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

#### Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- bladder cancer: recent studies have showed an increased risk of bladder cancer in patients taking pioglitazone (hazard ratio 2.64)

#### NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months

A 45-year-old man presents to the Emergency Department stating he has drunk a bottle of antifreeze. Which one of the following features are least associated with this kind of poisoning?

<input type="radio"/>	A. Metabolic acidosis with high anion gap
<input type="radio"/>	B. Acute renal failure
<input type="radio"/>	C. Hypertension
<input type="radio"/>	D. Confusion
<input type="radio"/>	E. Loss of vision

[Next question](#)

Loss of vision is seen in methanol rather than ethylene glycol poisoning

### Ethylene glycol toxicity

Ethylene glycol is a type of alcohol used as a coolant or antifreeze

Features of toxicity are divided into 3 stages:

- Stage 1: symptoms similar to alcohol intoxication: confusion, slurred speech, dizziness
- Stage 2: metabolic acidosis with high anion gap and high osmolar gap. Also tachycardia, hypertension
- Stage 3: acute renal failure

Management has changed in recent times

- ethanol has been used for many years
- works by competing with ethylene glycol for the enzyme alcohol dehydrogenase
- this limits the formation of toxic metabolites (e.g. glycoaldehyde and glycolic acid) which are responsible for the haemodynamic/metabolic features of poisoning
- **fomepizole**, an inhibitor of alcohol dehydrogenase, is now used first-line in preference to ethanol
- haemodialysis also has a role in refractory cases



Which one of the following is not a recognised indication for the use of octreotide?

<input type="radio"/>	A. Acute variceal haemorrhage
<input type="radio"/>	B. Acromegaly
<input type="radio"/>	C. VIPoma
<input type="radio"/>	D. Carcinoid syndrome
<input type="radio"/>	E. Hepatic encephalopathy

Next question

## Octreotide

### Overview

- long-acting analogue of somatostatin
- somatostatin is released from D cells of pancreas and inhibits the release of growth hormone, glucagon and insulin

### Uses

- acute treatment of variceal haemorrhage
- acromegaly
- carcinoid syndrome
- prevent complications following pancreatic surgery
- VIPomas

### Adverse effects

- gallstones (secondary to biliary stasis)

Which one of the following adverse effects is most likely to be seen in patients taking ciclosporin?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Hypertension        |
| <input type="radio"/> | B. Hypokalaemia        |
| <input type="radio"/> | C. Alopecia            |
| <input type="radio"/> | D. Dehydration         |
| <input type="radio"/> | E. Atrophy of the gums |

Next question

Ciclosporin side-effects: everything is increased - fluid, BP,  $K^+$ , hair, gums, glucose

## Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphatase that activates various transcription factors in T cells

Adverse effects of ciclosporin (note how everything is increased - fluid, BP,  $K^+$ , hair, gums, glucose)

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- gingival hyperplasia
- tremor
- impaired glucose tolerance

Interestingly for an immunosuppressant, ciclosporin is noted by the BNF to be 'virtually non-myelotoxic'.

## Indications

- following organ transplantation
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- ulcerative colitis
- pure red cell aplasia

Which one of the following enzymes is involved in phase I drug metabolism?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. UDP-glucuronosyl transferases |
| <input type="radio"/> | B. Pyruvate carboxylase          |
| <input type="radio"/> | C. Succinic dehydrogenase        |
| <input type="radio"/> | D. N-acetyl transferases         |
| <input type="radio"/> | E. Alcohol dehydrogenase         |

Next question

### Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

### First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are needed orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil
- isoprenaline
- testosterone
- hydrocortisone

Questions concerning zero-order kinetics and acetylator status are also common in the exam

## **Zero-order kinetics**

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

## **Acetylator status**

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

Which one of the following is least recognised as an adverse effect of taking bendroflumethiazide?

<input type="radio"/>	A. Photosensitivity rash
<input type="radio"/>	B. Agranulocytosis
<input type="radio"/>	C. Hypokalaemia
<input type="radio"/>	D. Pancreatitis
<input type="radio"/>	E. Hirsutism

Next question

### Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide was in the management of hypertension but recent NICE guidelines now recommend other thiazide-like diuretics such as indapamide and chlortalidone.

#### Common adverse effects

- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

#### Rare adverse effects

- thrombocytopaenia
- agranulocytosis
- photosensitivity rash
- pancreatitis

(An eagle eyed user noticed that this entry is very similar to the Wikipedia one. I can assure you that the material has been cut-and-pasted from passmedicine to Wikipedia, and not vice-versa! Note the English spellings of hyponatraemia etc. Check the Wikipedia 'history' page for more details.)

Which one of the following drugs cannot be cleared by haemodialysis?

<input type="radio"/>	A. Aspirin
<input type="radio"/>	B. Tricyclics
<input type="radio"/>	C. Lithium
<input type="radio"/>	D. Barbiturates
<input type="radio"/>	E. Aminophylline

Next question

### Haemodialysis in overdose

Drugs that can be cleared with haemodialysis - mnemonic: BLAST

- Barbiturate
- Lithium
- Alcohol (inc methanol, ethylene glycol)
- Salicylates
- Theophyllines (charcoal haemoperfusion is preferable)

Drugs which cannot be cleared with haemodialysis include

- tricyclics
- benzodiazepines
- dextropropoxyphene (Co-proxamol)
- digoxin
- beta-blockers

A 62-year-old woman who is known to have metastatic breast cancer presents with increasing shortness of breath. She is currently receiving a chemotherapy regime. On examination she has a third heart sound and the apex beat is displaced to the 6th intercostal space, anterior axillary line. Which one of the following chemotherapeutic agents is most likely to be responsible?

- ☐ A. Paclitaxel
- ☐ B. Docetaxel
- ☐ C. Bleomycin
- ☐ D. Dactinomycin
- ☐ E. Doxorubicin

### Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

A 67-year-old man with a history of atrial fibrillation and ischaemic heart disease presents with symptoms consistent with a chest infection. His current medication includes amiodarone, warfarin and simvastatin. Which one of the following antibiotics is it most important to avoid if possible?

<input type="radio"/>	A. Trimethoprim
<input type="radio"/>	B. Co-amoxiclav
<input type="radio"/>	C. Cefaclor
<input type="radio"/>	D. Levofloxacin
<input type="radio"/>	E. Erythromycin

[Next question](#)

Erythromycin may potentially interact with amiodarone, warfarin and simvastatin. Levofloxacin reacts to a lesser extent with both amiodarone and warfarin.

## Macrolides

Erythromycin was the first macrolide used clinically. Newer examples include clarithromycin and azithromycin.

Macrolides act by inhibiting bacterial protein synthesis. If pushed to give an answer they are bacteriostatic in nature, but in reality this depends on the dose and type of organism being treated.

### Adverse effects

- gastrointestinal side-effects are common. Nausea is less common with clarithromycin than erythromycin
- cholestatic jaundice: risk may be reduced if erythromycin stearate is used
- P450 inhibitor (see below)

### Common interactions

- statins should be stopped whilst taking a course of macrolides. Macrolides inhibit the cytochrome P450 isoenzyme CYP3A4 that metabolises statins. Taking macrolides concurrently with statins significantly increases the risk of myopathy and rhabdomyolysis.



A 46-year-old man with a history of hyperlipidaemia is reviewed in clinic. He is currently taking simvastatin 10mg on but his cholesterol level remains high. Previous attempts to increase the dose of simvastatin have resulted in myalgia. Given the history of myalgia, which lipid-regulating drug should be avoided?

- ☐ A. Nicotinic acid
- ☐ B. Bezafibrate
- ☐ C. Colestyramine
- ☐ D. Omega-3 fatty acid
- ☐ E. Ezetimibe

Next question

Tough question as both fibrates and nicotinic acid have been associated with myositis, especially when combined with a statin. However, the Committee on Safety of Medicines has produced guidance which specifically warns about the concomitant prescription of fibrates with statins in relation to muscle toxicity

### Hyperlipidaemia: drug adverse effects

The following table compares the side-effects of drugs used in hyperlipidaemia:

Drugs	Adverse effects
Statins (HMG CoA reductase inhibitors)	Myositis, deranged LFTs
Ezetimibe	Headache
Nicotinic acid	Flushing, myositis
Fibrates	Myositis, pruritus, cholestasis
Anion-exchange resins	GI side-effects

Which one of the following ECG changes is most consistent with a tricyclic overdose?

<input type="radio"/>	A. QRS widening
<input type="radio"/>	B. Bradycardia
<input type="radio"/>	C. Shortening of QT interval
<input type="radio"/>	D. First degree heart block
<input type="radio"/>	E. ST elevation

### Tricyclic overdose

Overdose of tricyclic antidepressants is a common presentation to emergency departments. Amitriptyline and dosulepin (dothiepin) are particularly dangerous in overdose.

Early features relate to anticholinergic properties: dry mouth, dilated pupils, agitation, sinus tachycardia, blurred vision.

Features of severe poisoning include:

- arrhythmias
- seizures
- metabolic acidosis
- coma

ECG changes include:

- sinus tachycardia
- widening of QRS
- prolongation of QT interval

Widening of QRS > 100ms is associated with an increased risk of seizures whilst QRS > 160ms is associated with ventricular arrhythmias

### Management

- IV bicarbonate may reduce the risk of seizures and arrhythmias in severe toxicity
- arrhythmias: class 1a (e.g. Quinidine) and class Ic antiarrhythmics (e.g. Flecainide) are contraindicated as they prolong depolarisation. Class III drugs such as amiodarone should also be avoided as they prolong the QT interval. Response to lignocaine is variable and it should be emphasized that correction of acidosis is the first line in management of tricyclic induced arrhythmias
- dialysis is ineffective in removing tricyclics

What is the minimum steroid intake a patient should be taking before they are offered osteoporosis prophylaxis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Equivalent of prednisolone 10 mg or more each day for 6 months  |
| <input type="radio"/> | B. Equivalent of prednisolone 7.5 mg or more each day for 6 weeks  |
| <input type="radio"/> | C. Equivalent of prednisolone 5 mg or more each day for 6 weeks    |
| <input type="radio"/> | D. Equivalent of prednisolone 7.5 mg or more each day for 3 months |
| <input type="radio"/> | E. Equivalent of prednisolone 10 mg or more each day for 6 weeks   |

Next question

### Osteoporosis: glucocorticoid-induced

Patients who take the equivalent of prednisolone 7.5 mg or more each day for 3 months or longer should be assessed and where necessary given prophylactic treatment

Assessment for treatment - patients taking the equivalent of prednisolone 7.5 mg or more each day for 3 months, and one of the following

- are over the age of 65 years
- have a history of a fragility fracture
- have a T-score less than - 1.5 SD

### Treatment

- first-line: oral bisphosphonate
- second-line: alfacalcidol or calcitriol

A 37-year-old who is 38 weeks pregnancy is an inpatient on the obstetric ward for the management of pre-eclampsia. Blood pressure is 172/114 mmHg and urine dipstick shows proteinuria +++. A decision has been made to start magnesium sulphate therapy as she is deemed at risk of eclampsia. Of the following options, which are the most important parameters to monitor whilst the patient is receiving magnesium?

- ☐ A. Blood sugar + pulse rate
- ☐ B. Reflexes + respiratory rate
- ☐ C. Blood sugar + respiratory rate
- ☐ D. Reflexes + pulse rate
- ☐ E. Glasgow coma scale + pulse rate

[Next question](#)

Magnesium sulphate - monitor reflexes + respiratory rate

## Eclampsia

Eclampsia may be defined as the development of seizures in association pre-eclampsia. To recap, pre-eclampsia is defined as:

- condition seen after 20 weeks gestation
- pregnancy-induced hypertension
- proteinuria

Magnesium sulphate is used to both prevent seizures in patients with severe pre-eclampsia and treat seizures once they develop. Guidelines on its use suggest the following:

- should be given once a decision to deliver has been made
- in eclampsia an IV bolus of 4g over 5-10 minutes should be given followed by an infusion of 1g / hour
- urine output, reflexes, respiratory rate and oxygen saturations should be monitored during treatment
- treatment should continue for 24 hours after last seizure or delivery (around 40% of seizures occur post-partum)

Other important aspects of treating severe pre-eclampsia/eclampsia include fluid restriction to avoid the potentially serious consequences of fluid overload

A 39-year-old woman who has recently been diagnosed with hypertension comes for review. She is sexually active but does not currently use any form of contraception other than barrier methods. Which one of the following medications should be avoided?

- |                       |                |
|-----------------------|----------------|
| <input type="radio"/> | A. Hydralazine |
| <input type="radio"/> | B. Nifedipine  |
| <input type="radio"/> | C. Methyldopa  |
| <input type="radio"/> | D. Labetalol   |
| <input type="radio"/> | E. Lisinopril  |

[Next question](#)

When prescribing this woman should be treated as if she were pregnant given the absence of effective contraception. ACE inhibitors such as lisinopril are known teratogens and must be avoided.

### Prescribing in pregnant patients

Very few drugs are known to be completely safe in pregnancy. The list below largely comprises of those known to be harmful. Some countries have developed a grading system - see the link.

#### Antibiotics

- tetracyclines
- aminoglycosides
- sulphonamides and trimethoprim
- quinolones: the BNF advises to avoid due to arthropathy in some animal studies

#### Other drugs

- ACE inhibitors, angiotensin II receptor antagonists
- statins
- warfarin
- sulfonylureas
- retinoids (including topical)
- cytotoxic agents

The majority of antiepileptics including valproate, carbamazepine and phenytoin are known to be potentially harmful. The decision to stop such treatments however is difficult as uncontrolled epilepsy is also a risk

Which one of the following may be associated with an increased risk of venous thromboembolism?

<input type="radio"/>	A. Fluoxetine
<input type="radio"/>	B. Selegiline
<input type="radio"/>	C. Diazepam
<input type="radio"/>	D. Amitriptyline
<input type="radio"/>	E. Olanzapine

Next question

### Venous thromboembolism: risk factors

Common predisposing factors include malignancy, pregnancy and the period following an operation. The comprehensive list below is partly based on the 2010 SIGN venous thromboembolism (VTE) guidelines:

#### General

- increased risk with advancing age
- obesity
- family history of VTE
- pregnancy (especially puerperium)
- immobility
- hospitalisation
- anaesthesia
- central venous catheter: femoral >> subclavian

#### Underlying conditions

- malignancy
- thrombophilia: e.g. Activated protein C resistance, protein C and S deficiency
- heart failure
- antiphospholipid syndrome
- Behcet's
- polycythaemia
- nephrotic syndrome
- sickle cell disease
- paroxysmal nocturnal haemoglobinuria
- hyperviscosity syndrome
- homocystinuria

## Medication

- combined oral contraceptive pill: 3rd generation more than 2nd generation
- hormone replacement therapy
- raloxifene and tamoxifen
- antipsychotics (especially olanzapine) have recently been shown to be a risk factor

SIGN also state that the following are risk factors for recurrent VTE:

- previous unprovoked VTE
- male sex
- obesity
- thrombophilias

A 54-year-old female is being investigated for a macrocytic anaemia. Bloods test reveal a low vitamin B12 level. Which one of the following medications may be contributing to this?

<input type="radio"/>	A. Bendroflumethiazide
<input type="radio"/>	B. Digoxin
<input type="radio"/>	C. Amiodarone
<input type="radio"/>	D. Sodium valproate
<input type="radio"/>	E. Metformin

### Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

#### Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

#### Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis\* with severe liver disease or renal failure

#### Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is  $> 130 \mu\text{mol/l}$  and stopping metformin if  $> 150 \mu\text{mol/l}$
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome



### Question 127 of 265

A 71-year-old woman is prescribed ondansetron to help treat nausea which has not responded to either metoclopramide or cyclizine. What is the mechanism of action of ondansetron?

<input type="radio"/>	A. 5-HT3 antagonist
<input type="radio"/>	B. 5-HT2 antagonist
<input type="radio"/>	C. Dopamine antagonist
<input type="radio"/>	D. NK1 receptor antagonist
<input type="radio"/>	E. Antihistamine

[Next question](#)

Examples of dopamine antagonists include metoclopramide and domperidone.

### 5-HT3 antagonists

5-HT3 antagonists are antiemetics used mainly in the management of chemotherapy related nausea.

Examples

- ondansetron
- granisetron

A 20-year-old student drinks around 500 ml of vodka at a party. The next morning he feels thirsty and finds he is passing more urine than normal. Which one of the following best explains why people who drink excessive amounts alcohol develop polyuria?

<input type="radio"/>	A. Ethanol inhibits ADH secretion
<input type="radio"/>	B. Ethanol induces vasoconstriction of the renal arteries
<input type="radio"/>	C. Ethanol increases aquaporin proteins in the proximal convoluted tubule
<input type="radio"/>	D. Osmotic diuresis induced by ethanol
<input type="radio"/>	E. Supratentorial reflex to cleanse the body of toxins

[Next question](#)

Ethanol reduces the calcium-dependent secretion of anti-diuretic hormone (ADH) by blocking channels in the neurohypophyseal nerve terminal.

Nausea associated with hangovers is mainly due to vagal stimulation to the vomiting centre. Following a particular severe episode of alcohol excess people may experience tremors. These are due to increased glutamate production by neurones to compensate for the previous inhibition by ethanol.

### Alcohol - problem drinking: management

#### Nutritional support

- SIGN recommends alcoholic patients should receive oral thiamine if their 'diet may be deficient'

#### Drugs used

- benzodiazepines for acute withdrawal
- disulfam: promotes abstinence - alcohol intake causes severe reaction due to inhibition of acetaldehyde dehydrogenase. Patients should be aware that even small amounts of alcohol (e.g. In perfumes, foods, mouthwashes) can produce severe symptoms. Contraindications include ischaemic heart disease and psychosis
- acamprosate: reduces craving, known to be a weak antagonist of NMDA receptors, improves abstinence in placebo controlled trials

A patient is started on finasteride for the treatment of benign prostatic hyperplasia. How long should the patient be told that treatment may take to be effective?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Within 8 hours of taking the tablet |
| <input type="radio"/> | B. Within 3 days                       |
| <input type="radio"/> | C. Up to 7 days                        |
| <input type="radio"/> | D. Up to 4 weeks                       |
| <input type="radio"/> | E. Up to 6 months                      |

[Next question](#)

Finasteride treatment of BPH may take 6 months before results are seen

## Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition seen in older men.

### Risk factors

- age: around 50% of 50-year-old men will have evidence of BPH and 30% will have symptoms. Around 80% of 80-year-old men have evidence of BPH
- ethnicity: black > white > Asian

BPH typically presents with lower urinary tract symptoms (LUTS), which may be categorised into:

- voiding symptoms (obstructive): weak or intermittent urinary flow, straining, hesitancy, terminal dribbling and incomplete emptying
- storage symptoms (irritative) urgency, frequency, urgency incontinence and nocturia
- post-micturition: dribbling
- complications: urinary tract infection, retention, obstructive uropathy

### Management options

- watchful waiting
- medication: alpha-1 antagonists, 5 alpha-reductase inhibitors. The use of combination therapy was supported by the Medical Therapy Of Prostatic Symptoms (MTOPS) trial
- surgery: transurethral resection of prostate (TURP)

Alpha-1 antagonists e.g. tamsulosin, alfuzosin

- decrease smooth muscle tone (prostate and bladder)
- considered first-line, improve symptoms in around 70% of men
- adverse effects: dizziness, postural hypotension, dry mouth, depression

5 alpha-reductase inhibitors e.g. finasteride

- block the conversion of testosterone to dihydrotestosterone (DHT), which is known to induce BPH
- unlike alpha-1 antagonists causes a reduction in prostate volume and hence may slow disease progression. This however takes time and symptoms may not improve for 6 months. They may also decrease PSA concentrations by up to 50%
- adverse effects: erectile dysfunction, reduced libido, ejaculation problems, gynaecomastia

A 72-year-old man is prescribed a dipyridamole in addition to aspirin following an ischaemic stroke. What is the mechanism of action of dipyridamole?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Phosphodiesterase inhibitor                   |
| <input type="radio"/> | B. Glycoprotein IIb/IIIa inhibitor               |
| <input type="radio"/> | C. Inhibits ADP binding to its platelet receptor |
| <input type="radio"/> | D. Agonist of thromboxane synthase               |
| <input type="radio"/> | E. Irreversibly acetylating Cyclooxygenase       |

[Next question](#)

Dipyridamole inhibits phosphodiesterase

### Dipyridamole

Dipyridamole is an antiplatelet mainly used in combination with aspirin after an ischaemic stroke or transient ischaemic attack.

#### Mechanism of action

- inhibits phosphodiesterase, elevating platelet cAMP levels which in turn reduce intracellular calcium levels
- other actions include reducing cellular uptake of adenosine and inhibition of thromboxane synthase

A 26-year-old female is commenced on carbamazepine for complex partial seizures. She has no previous medical history of note and consumes a moderate amount of alcohol. Three months later she is admitted due to series of seizures and carbamazepine levels are noted to be subtherapeutic. A pill-count reveals the patient is fully compliant. What is the most likely explanation?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Auto-inhibition of liver enzymes |
| <input type="radio"/> | B. Prescription of omeprazole       |
| <input type="radio"/> | C. Prescription of fluoxetine       |
| <input type="radio"/> | D. Auto-induction of liver enzymes  |
| <input type="radio"/> | E. Alcohol binge                    |

Carbamazepine is an inducer of the P450 system. This in turn increases the metabolism of carbamazepine itself - auto-induction

### P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

A 23-year-old female is commenced on varenicline to help her stop smoking. Which one of the following adverse effects is most likely to occur?

<input type="radio"/>	A. Vivid dreams
<input type="radio"/>	B. Nausea
<input type="radio"/>	C. Constipation
<input type="radio"/>	D. Insomnia
<input type="radio"/>	E. Drug-induced lupus

[Next question](#)

Whilst all of the above adverse effects may occur nausea is the most common

### Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

#### Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

#### Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop
- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)

- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

## Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication



Which one of the following is an established indication for the use of Botulinum toxin?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Strabismus                                 |
| <input type="radio"/> | B. Hirschsprung's disease                     |
| <input type="radio"/> | C. Blepharospasm                              |
| <input type="radio"/> | D. Bell's palsy                               |
| <input type="radio"/> | E. Upper limb rigidity in Parkinson's disease |

Next question

### Botulinum toxin

As well as the well publicised cosmetic uses of Botulinum toxin ('Botox') there are also a number of licensed indications:

- blepharospasm
- hemifacial spasm
- focal spasticity including cerebral palsy patients, hand and wrist disability associated with stroke
- spasmodic torticollis
- severe hyperhidrosis of the axillae
- achalasia

Which one of the following drugs is most likely to cause impaired glucose tolerance?

<input type="radio"/>	A. Bezafibrate
<input type="radio"/>	B. Simvastatin
<input type="radio"/>	C. Nicotinic acid
<input type="radio"/>	D. Cholestyramine
<input type="radio"/>	E. Gemfibrozil

Next question

### Drug-induced impaired glucose tolerance

Drugs which are known to cause impaired glucose tolerance include:

- thiazides, furosemide (less common)
- steroids
- tacrolimus, ciclosporin
- interferon-alpha
- nicotinic acid
- atypical antipsychotics e.g. olanzapine

Beta-blockers cause a slight impairment of glucose tolerance. They should also be used with caution in diabetics as they can interfere with the metabolic and autonomic responses to hypoglycaemia

A 51-year-old homeless man is brought to the Emergency Department by an ambulance. He was found collapsed in the street. His friend reports that he has drink two litres of cheap spirits made with methanol. On arrival his GCS is 5, blood pressure 120 / 70 mmHg and pulse 90 / min. His airway is secured and oxygen given. What is the most appropriate treatment?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Ethanol            |
| <input type="radio"/> | B. Activated charcoal |
| <input type="radio"/> | C. Thiamine           |
| <input type="radio"/> | D. Fomepizole         |
| <input type="radio"/> | E. Haemodialysis      |

[Next question](#)

His low GCS level points to a severe overdose. Haemodialysis is therefore indicated. Other indications for haemodialysis in methanol poisoning include a methanol level > 0.5g/L, renal impairment and any visual disturbance.

### Methanol poisoning

Methanol poisoning causes both the effects associated with alcohol (intoxication, nausea etc) and also specific visual problems, including blindness. These effects are thought to be secondary to the accumulation of formic acid. The actual pathophysiology of methanol-associated visual loss is not fully understood but it is thought to be caused by a form of optic neuropathy

#### Management

- fomepizole or ethanol
- haemodialysis

A 67-year-old female is prescribed simvastatin for hyperlipidaemia. Which one of the following is most likely to interact with her medication?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Orange juice     |
| <input type="radio"/> | B. Apple juice      |
| <input type="radio"/> | C. Grapefruit juice |
| <input type="radio"/> | D. Cranberry juice  |
| <input type="radio"/> | E. Carrot juice     |

Next question

Grapefruit juice is a potent inhibitor of the cytochrome P450 enzyme CYP3A4

### Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

#### Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

#### Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk  $\geq 20\%$
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM  $> 40$ -years-old were prescribed statins. Now patients  $> 40$ -years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk  $< 20\%/10$  years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering\*

	<b>Total cholesterol (mmol/l)</b>	<b>LDL cholesterol</b>
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

\*current NICE guidelines do not recommend a target cholesterol in primary prevention

A 55-year-old female is admitted following an overdose of amitriptyline. On examination she has dilated pupils and is tachycardic at 160 bpm, with a blood pressure of 96/54 mmHg. ECG reveals a broad complex tachycardia. What is the most appropriate management?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. IV amiodarone    |
| <input type="radio"/> | B. IV bicarbonate   |
| <input type="radio"/> | C. IV magnesium     |
| <input type="radio"/> | D. DC cardioversion |
| <input type="radio"/> | E. Glucagon         |

[Next question](#)

Tricyclic overdose - give IV bicarbonate

Arrhythmias following tricyclic overdose are difficult to treat as many commonly used anti-arrhythmics are contraindicated. The use of sodium bicarbonate has been shown to be effective, even in patients who are not acidotic

### Tricyclic overdose

Overdose of tricyclic antidepressants is a common presentation to emergency departments. Amitriptyline and dosulepin (dothiepin) are particularly dangerous in overdose.

Early features relate to anticholinergic properties: dry mouth, dilated pupils, agitation, sinus tachycardia, blurred vision.

Features of severe poisoning include:

- arrhythmias
- seizures
- metabolic acidosis
- coma

ECG changes include:

- sinus tachycardia
- widening of QRS
- prolongation of QT interval

Widening of QRS > 100ms is associated with an increased risk of seizures whilst QRS > 160ms is associated

with ventricular arrhythmias

## Management

- IV bicarbonate may reduce the risk of seizures and arrhythmias in severe toxicity
- arrhythmias: class 1a (e.g. Quinidine) and class Ic antiarrhythmics (e.g. Flecainide) are contraindicated as they prolong depolarisation. Class III drugs such as amiodarone should also be avoided as they prolong the QT interval. Response to lignocaine is variable and it should be emphasized that correction of acidosis is the first line in management of tricyclic induced arrhythmias
- dialysis is ineffective in removing tricyclics

Which of the following drugs is least likely to be affected by a patient's acetylator status?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Hydralazine   |
| <input type="radio"/> | B. Isoniazid     |
| <input type="radio"/> | C. Rifampicin    |
| <input type="radio"/> | D. Procainamide  |
| <input type="radio"/> | E. Sulphonamides |

Next question

### Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

### First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are needed orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil
- isoprenaline
- testosterone
- hydrocortisone

Questions concerning zero-order kinetics and acetylator status are also common in the exam



## **Zero-order kinetics**

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

## **Acetylator status**

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

**Question 139 of 265**

Next

A 35-year-old man with a known history of peanut allergy is admitted to the Emergency Department with a swollen face. On examination blood pressure is 85/60 mmHg, pulse 120 bpm and there is a bilateral expiratory wheeze. What is the most appropriate form of adrenaline to give?

<input type="radio"/>	A. 10ml 1:10,000 IV
<input type="radio"/>	B. 0.5ml 1:1,000 IM
<input type="radio"/>	C. 0.5ml 1:10,000 IM
<input type="radio"/>	D. 5ml 1:1,000 IM
<input type="radio"/>	E. Nebulised adrenaline

Next question

Recommend Adult Life Support (ALS) adrenaline doses

- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

**Adrenaline**

Adrenaline is a sympathomimetic amine with both alpha and beta adrenergic stimulating properties

Indications

- anaphylaxis
- cardiac arrest

Recommend Adult Life Support (ALS) adrenaline doses

- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

Management of accidental injection

- local infiltration of phentolamine

A 19-year-old female is brought to the Emergency Department by her friends following a night out. Her friends state she has taken an unknown drug whilst out clubbing. Which one of the following features would most point towards the use of ecstasy?

<input type="radio"/>	A. Temperature of 39.5°C
<input type="radio"/>	B. Respiratory depression
<input type="radio"/>	C. Hypernatraemia
<input type="radio"/>	D. Miosis
<input type="radio"/>	E. Urinary incontinence

[Next question](#)

### Ecstasy poisoning

Ecstasy (MDMA, 3,4-Methylenedioxymethamphetamine) use became popular in the 1990's during the emergence of dance music culture

#### Clinical features

- neurological: agitation, anxiety, confusion, ataxia
- cardiovascular: tachycardia, hypertension
- hyponatraemia
- hyperthermia
- rhabdomyolysis

#### Management

- supportive
- dantrolene may be used for hyperthermia if simple measures fail

A 72-year-old man who is having trouble sleeping is prescribed temazepam. What is the mechanism of action of temazepam?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Inhibits the effect of acetylcholine           |
| <input type="radio"/> | B. Enhances the effect of gamma-aminobutyric acid |
| <input type="radio"/> | C. Inhibits the effect gamma-aminobutyric acid    |
| <input type="radio"/> | D. Inhibits the effect of glutamate               |
| <input type="radio"/> | E. Inhibits the effect of noradrenaline           |

[Next question](#)

Benzodiazepines enhance the effect of GABA, the main inhibitory neurotransmitter

## Benzodiazepines

Benzodiazepines enhance the effect of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). They therefore are used for a variety of purposes:

- sedation
- hypnotic
- anxiolytic
- anticonvulsant
- muscle relaxant

Patients commonly develop a tolerance and dependence to benzodiazepines and care should therefore be exercised on prescribing these drugs. The Committee on Safety of Medicines advises that benzodiazepines are only prescribed for a short period of time (2-4 weeks).

The BNF gives advice on how to withdraw a benzodiazepine. The dose should be withdrawn in steps of about 1/8 (range 1/10 to 1/4) of the daily dose every fortnight. A suggested protocol for patients experiencing difficulty is given:

- switch patients to the equivalent dose of diazepam
- reduce dose of diazepam every 2-3 weeks in steps of 2 or 2.5 mg
- time needed for withdrawal can vary from 4 weeks to a year or more

If patients withdraw too quickly from benzodiazepines they may experience benzodiazepine withdrawal

syndrome, a condition very similar to alcohol withdrawal syndrome. This may occur up to 3 weeks after stopping a long-acting drug. Features include:

- insomnia
- irritability
- anxiety
- tremor
- loss of appetite
- tinnitus
- perspiration
- perceptual disturbances
- seizures

A patient presents to the Emergency Department following the development of an urticarial skin rash following the introduction of a new drug. Which one of the following is most likely to be responsible?

<input type="radio"/>	A. Omeprazole
<input type="radio"/>	B. Sodium valproate
<input type="radio"/>	C. Aspirin
<input type="radio"/>	D. Paracetamol
<input type="radio"/>	E. Simvastatin

[Next question](#)

Aspirin is a common cause of urticaria

Although all medications can potentially cause urticaria it is commonly seen secondary to aspirin

#### Drug causes of urticaria

The following drugs commonly cause urticaria:

- aspirin
- penicillins
- NSAIDs
- opiates

A 59-year-old man with a history of type 2 diabetes mellitus and benign prostatic hypertrophy develops urinary retention associated with acute renal failure. Which one of the following drugs should be discontinued?

<input type="radio"/>	A. Gliclazide
<input type="radio"/>	B. Paroxetine
<input type="radio"/>	C. Atenolol
<input type="radio"/>	D. Metformin
<input type="radio"/>	E. Finasteride

As the patient has developed acute renal failure metformin should be stopped due to the risk of lactic acidosis. In the long term paroxetine may also need to be stopped as SSRIs can contribute to urinary retention.

### Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

#### Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

#### Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis\* with severe liver disease or renal failure

#### Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is  $> 130 \mu\text{mol/l}$  and stopping metformin if  $> 150 \mu\text{mol/l}$
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Which one of the following is least associated with cocaine toxicity?

<input type="radio"/>	A. Metabolic alkalosis
<input type="radio"/>	B. Hyperthermia
<input type="radio"/>	C. Psychosis
<input type="radio"/>	D. Rhabdomyolysis
<input type="radio"/>	E. Seizures

## Cocaine

Cocaine use may cause a wide variety of adverse effects

### Cardiovascular effects

- myocardial infarction
- both tachycardia and bradycardia may occur
- hypertension
- QRS widening and QT prolongation
- aortic dissection

### Neurological effects

- seizures
- mydriasis
- hypertonia
- hyperreflexia

### Psychiatric effects

- agitation
- psychosis
- hallucinations

### Others

- hyperthermia
- metabolic acidosis
- rhabdomyolysis



**Question 145 of 265**

Next

A 54-year-old man with a history of ischaemic heart disease is currently taking atorvastatin 40mg at night. A repeat lipid profile is ordered:

Total cholesterol	3.9 mmol/l
HDL	0.7 mmol/l
LDL	2.6 mmol/l
Triglycerides	1.2 mmol/l

What would be the most effective way of increasing HDL levels?

- ☐ A. Add nicotinic acid
- ☐ B. Add ezetimibe
- ☐ C. Switch atorvastatin to pravastatin
- ☐ D. Add bezafibrate
- ☐ E. Add colestyramine

Next question

Nicotinic acid increases HDL levels

**Nicotinic acid**

Nicotinic acid is used in the treatment of patients with hyperlipidaemia, although its use is limited by side-effects. As well as lowering cholesterol and triglyceride concentrations it also raises HDL levels

Adverse effects

- flushing
- impaired glucose tolerance
- myositis

Which one of the following features is least recognised in long-term lithium use?

- |                       |                |
|-----------------------|----------------|
| <input type="radio"/> | A. Alopecia    |
| <input type="radio"/> | B. Weight gain |
| <input type="radio"/> | C. Fine tremor |
| <input type="radio"/> | D. Goitre      |
| <input type="radio"/> | E. Diarrhoea   |

Next question

All the above side-effects, with the exception of alopecia, may be seen in patients taking lithium

## Lithium

Lithium is mood stabilising drug used most commonly prophylactically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys.

Mechanism of action - not fully understood, two theories:

- interferes with inositol triphosphate formation
- interferes with cAMP formation

Adverse effects

- nausea/vomiting, diarrhoea
- fine tremor
- polyuria (secondary to nephrogenic diabetes insipidus)
- thyroid enlargement, may lead to hypothyroidism
- ECG: T wave flattening/inversion
- weight gain

Monitoring of patients on lithium therapy

- inadequate monitoring of patients taking lithium is common - NICE and the National Patient Safety Agency (NPSA) have issued guidance to try and address this. As a result it is often an exam hot topic
- lithium blood level should 'normally' be checked every 3 months. Levels should be taken 12 hours post-dose
- thyroid and renal function should be checked every 6 months
- patients should be issued with an information booklet, alert card and record book

A patient is admitted with central chest pain and a diagnosis of non-ST elevation myocardial infarction is made. Aspirin and fondaparinux are given. What is the mechanism of action of fondaparinux?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Reversible direct thrombin inhibitor          |
| <input type="radio"/> | B. Glycoprotein IIb/IIIa receptor antagonist     |
| <input type="radio"/> | C. Inhibits antithrombin III                     |
| <input type="radio"/> | D. Inhibits ADP binding to its platelet receptor |
| <input type="radio"/> | E. Activates antithrombin III                    |

[Next question](#)

Fondaparinux works in a similar way to low-molecular weight heparin.

### Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive

- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

**Antithrombin** treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is  $> 265 \mu\text{mol/l}$  unfractionated heparin should be given.

**Clopidogrel** 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

**Coronary angiography** should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

<b>Aspirin</b>	Antiplatelet - inhibits the production of thromboxane A2
<b>Clopidogrel</b>	Antiplatelet - inhibits ADP binding to its platelet receptor
<b>Enoxaparin</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Fondaparinux</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Bivalirudin</b>	Reversible direct thrombin inhibitor

Which one of the following symptom is least associated with salicylate overdose?

<input type="radio"/>	A. Tremor
<input type="radio"/>	B. Tinnitus
<input type="radio"/>	C. Hyperventilation
<input type="radio"/>	D. Seizures
<input type="radio"/>	E. Nausea

### Salicylate overdose

A key concept for the exam is to understand that salicylate overdose leads to a mixed respiratory alkalosis and metabolic acidosis. Early stimulation of the respiratory centre leads to a respiratory alkalosis whilst later the direct acid effects of salicylates (combined with acute renal failure) may lead to an acidosis. In children metabolic acidosis tends to predominate

#### Features

- hyperventilation (centrally stimulates respiration)
- tinnitus
- lethargy
- sweating, pyrexia\*
- nausea/vomiting
- hyperglycaemia and hypoglycaemia
- seizures
- coma

#### Treatment

- general (ABC, charcoal)
- urinary alkalization is now rarely used - it is contraindicated in cerebral and pulmonary oedema with most units now proceeding straight to haemodialysis in cases of severe poisoning
- haemodialysis

#### Indications for haemodialysis in salicylate overdose

- serum concentration > 700mg/L
- metabolic acidosis resistant to treatment
- acute renal failure
- pulmonary oedema
- seizures
- coma

\*salicylates cause the uncoupling of oxidative phosphorylation leading to decreased adenosine triphosphate production, increased oxygen consumption and increased carbon dioxide and heat production

Which one of the following drugs is least likely to cause gynaecomastia?

<input type="radio"/>	A. Spironolactone
<input type="radio"/>	B. Sodium valproate
<input type="radio"/>	C. Digoxin
<input type="radio"/>	D. Cimetidine
<input type="radio"/>	E. Anabolic steroids

Next question

Whilst sodium valproate may rarely causes gynaecomastia it is much more common after taking the other listed drugs.

### Gynaecomastia

Gynaecomastia describes an abnormal amount of breast tissue in males and is usually caused by an increased oestrogen:androgen ratio. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

#### Causes of gynaecomastia

- physiological: normal in puberty
- syndromes with androgen deficiency: Kallman's, Klinefelter's
- testicular failure: e.g. mumps
- liver disease
- testicular cancer e.g. seminoma secreting hCG
- ectopic tumour secretion
- hyperthyroidism
- haemodialysis
- drugs: see below

#### Drug causes of gynaecomastia

- spironolactone (most common drug cause)
- cimetidine
- digoxin
- cannabis
- finasteride
- gonadorelin analogues e.g. Goserelin, buserelin
- oestrogens, anabolic steroids

#### Very rare drug causes of gynaecomastia

- tricyclics
- isoniazid
- calcium channel blockers
- heroin
- busulfan
- methyldopa

A 62-year-old man is reviewed in diabetes clinic. His glycaemic control is poor despite weight loss, adherence to a diabetic diet and his current diabetes medications. He has no other past medical history of note. Which one of the following medications would increase insulin sensitivity?

<input type="radio"/>	A. Repaglinide
<input type="radio"/>	B. Tolbutamide
<input type="radio"/>	C. Pioglitazone
<input type="radio"/>	D. Acarbose
<input type="radio"/>	E. Gliclazide

[Next question](#)

### Thiazolidinediones

Thiazolidinediones are a new class of agents used in the treatment of type 2 diabetes mellitus. They are agonists to the PPAR-gamma receptor and reduce peripheral insulin resistance. Rosiglitazone was withdrawn in 2010 following concerns about the cardiovascular side-effect profile.

The PPAR-gamma receptor is an intracellular nuclear receptor. Its natural ligands are free fatty acids and it is thought to control adipocyte differentiation and function.

#### Adverse effects

- weight gain
- liver impairment: monitor LFTs
- fluid retention - therefore contraindicated in heart failure. The risk of fluid retention is increased if the patient also takes insulin
- recent studies have indicated an increased risk of fractures
- bladder cancer: recent studies have showed an increased risk of bladder cancer in patients taking pioglitazone (hazard ratio 2.64)

#### NICE guidance on thiazolidinediones

- only continue if there is a reduction of > 0.5 percentage points in HbA1c in 6 months



A 52-year-old homeless man is admitted with suspected ethylene glycol toxicity. Following admission to the High Dependency Unit it is decided to give fomepizole. What is the mechanism of action of fomepizole?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Competitive inhibitor of aldehyde dehydrogenase |
| <input type="radio"/> | B. Binds to glycoaldehyde                          |
| <input type="radio"/> | C. Binds to glycolic acid                          |
| <input type="radio"/> | D. Promotes renal excretion of ethylene glycol     |
| <input type="radio"/> | E. Competitive inhibitor of alcohol dehydrogenase  |

[Next question](#)

### Ethylene glycol toxicity

Ethylene glycol is a type of alcohol used as a coolant or antifreeze

Features of toxicity are divided into 3 stages:

- Stage 1: symptoms similar to alcohol intoxication: confusion, slurred speech, dizziness
- Stage 2: metabolic acidosis with high anion gap and high osmolar gap. Also tachycardia, hypertension
- Stage 3: acute renal failure

Management has changed in recent times

- ethanol has been used for many years
- works by competing with ethylene glycol for the enzyme alcohol dehydrogenase
- this limits the formation of toxic metabolites (e.g. glycoaldehyde and glycolic acid) which are responsible for the haemodynamic/metabolic features of poisoning
- **fomepizole**, an inhibitor of alcohol dehydrogenase, is now used first-line in preference to ethanol
- haemodialysis also has a role in refractory cases

A 47-year-old lorry driver presents following the development of a widespread urticarial rash. This is associated with pruritus. What is the most appropriate medication to help relieve the itch?

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. Cetirizine     |
| <input type="radio"/> | B. Loratadine     |
| <input type="radio"/> | C. Chlorphenamine |
| <input type="radio"/> | D. Ranitidine     |
| <input type="radio"/> | E. Alimemazine    |

[Next question](#)

The obvious concern in a lorry driver is drowsiness. Of the non-sedating antihistamines there is some evidence that cetirizine causes more drowsiness than loratadine

### Antihistamines

Antihistamines are of value in the treatment of allergic rhinitis and urticaria. Of the non-sedating antihistamines there is some evidence that cetirizine may cause more drowsiness than other drugs in the class

Which one of the following is a mixed alpha and beta adrenoceptor antagonist?

<input type="radio"/>	A. Doxazosin
<input type="radio"/>	B. Phenoxybenzamine
<input type="radio"/>	C. Yohimbine
<input type="radio"/>	D. Propranolol
<input type="radio"/>	E. Carvedilol

Next question

### Adrenoceptor antagonists

#### Alpha antagonists

- alpha-1: doxazosin
- alpha-1a: tamsulosin - acts mainly on urogenital tract
- alpha-2: yohimbine
- non-selective: phenoxybenzamine (previously used in peripheral arterial disease)

#### Beta antagonists

- beta-1: atenolol
- non-selective: propranolol

Carvedilol and labetalol are mixed alpha and beta antagonists

Which one of the following is an absolute contraindication to combined oral contraceptive pill use?

<input type="radio"/>	A. Controlled hypertension
<input type="radio"/>	B. History of cholestasis
<input type="radio"/>	C. Women more than 35 years old and smoking more than 15 cigarettes/day
<input type="radio"/>	D. BMI of 38 kg/m <sup>2</sup>
<input type="radio"/>	E. Migraine without aura

### Combined oral contraceptive pill: contraindications

The decision of whether to start a woman on the combined oral contraceptive pill is now guided by the UK Medical Eligibility Criteria (UKMEC). This scale categorises the potential cautions and contraindications according to a four point scale, as detailed below:

- UKMEC 1: a condition for which there is no restriction for the use of the contraceptive method
- UKMEC 2: advantages generally outweigh the disadvantages
- UKMEC 3: disadvantages generally outweigh the advantages
- UKMEC 4: represents an unacceptable health risk

Examples of UKMEC 3 conditions include

- more than 35 years old and smoking less than 15 cigarettes/day
- BMI > 35 kg/m<sup>2</sup>\*
- migraine without aura and more than 35 years old
- family history of thromboembolic disease in first degree relatives < 45 years
- controlled hypertension
- immobility e.g. wheel chair use
- breast feeding 6 weeks - 6 months postpartum

Examples of UKMEC 4 conditions include

- more than 35 years old and smoking more than 15 cigarettes/day
- migraine with aura
- history of thromboembolic disease or thrombogenic mutation
- history of stroke or ischaemic heart disease
- breast feeding < 6 weeks post-partum
- uncontrolled hypertension
- breast cancer
- major surgery with prolonged immobilisation

Diabetes mellitus diagnosed > 20 years ago is classified as UKMEC 3 or 4 depending on severity

\*The UKMEC 4 rating for a BMI > 40 kg/m<sup>2</sup> was removed in 2009.

A 76-year-old man presents with lower urinary tract symptoms. Following a digital rectal examination and prostate specific antigen test a diagnosis of benign prostatic hyperplasia is made and finasteride is started. What is the mechanism of action of this drug?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Alpha-1 antagonist   |
| <input type="radio"/> | B. 5-alpha receptor antagonist                                |
| <input type="radio"/> | C. Testosterone receptor antagonist                           |
| <input type="radio"/> | D. Alpha-1 agonists   |
| <input type="radio"/> | E. Inhibits conversion of testosterone to dihydrotestosterone |

[Next question](#)

Finasteride: 5 alpha-reductase inhibitor - inhibits conversion of testosterone to dihydrotestosterone

## Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition seen in older men.

### Risk factors

- age: around 50% of 50-year-old men will have evidence of BPH and 30% will have symptoms. Around 80% of 80-year-old men have evidence of BPH
- ethnicity: black > white > Asian

BPH typically presents with lower urinary tract symptoms (LUTS), which may be categorised into:

- voiding symptoms (obstructive): weak or intermittent urinary flow, straining, hesitancy, terminal dribbling and incomplete emptying
- storage symptoms (irritative) urgency, frequency, urgency incontinence and nocturia
- post-micturition: dribbling
- complications: urinary tract infection, retention, obstructive uropathy

### Management options

- watchful waiting
- medication: alpha-1 antagonists, 5 alpha-reductase inhibitors. The use of combination therapy was supported by the Medical Therapy Of Prostatic Symptoms (MTOPS) trial
- surgery: transurethral resection of prostate (TURP)

Alpha-1 antagonists e.g. tamsulosin, alfuzosin

- decrease smooth muscle tone (prostate and bladder)
- considered first-line, improve symptoms in around 70% of men
- adverse effects: dizziness, postural hypotension, dry mouth, depression

5 alpha-reductase inhibitors e.g. finasteride

- block the conversion of testosterone to dihydrotestosterone (DHT), which is known to induce BPH
- unlike alpha-1 antagonists causes a reduction in prostate volume and hence may slow disease progression. This however takes time and symptoms may not improve for 6 months. They may also decrease PSA concentrations by up to 50%
- adverse effects: erectile dysfunction, reduced libido, ejaculation problems, gynaecomastia

A 65-year-old man with a history of type 2 diabetes mellitus and ischaemic heart disease presents with erectile dysfunction. It is decided to try sildenafil therapy. Which one of the following existing medications may be continued without making any adjustments?

<input type="radio"/>	A. GTN spray
<input type="radio"/>	B. Nicorandil
<input type="radio"/>	C. Nateglinide
<input type="radio"/>	D. Doxazosin
<input type="radio"/>	E. Isosorbide mononitrate

[Next question](#)

The BNF recommends avoiding alpha-blockers for 4 hours after sildenafil

### Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

#### Contraindications

- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

#### Side-effects

- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects
- headache

Which of the following is least likely to be a precipitating factor in digoxin toxicity?

- |                       |                    |
|-----------------------|--------------------|
| <input type="radio"/> | A. Hyponatraemia   |
| <input type="radio"/> | B. Hypocalcaemia   |
| <input type="radio"/> | C. Hypokalaemia    |
| <input type="radio"/> | D. Hypothermia     |
| <input type="radio"/> | E. Hypomagnesaemia |

Next question

Hyper-, not hypocalcaemia may be a precipitating factor in digoxin toxicity

### Digoxin and digoxin toxicity

Digoxin is a cardiac glycoside now mainly used for rate control in the management of atrial fibrillation. As it has positive inotropic properties it is sometimes used for improving symptoms (but not mortality) in patients with heart failure.

Mechanism of action

- decreases conduction through the atrioventricular node which slows the ventricular rate in atrial fibrillation and flutter
- increases the force of cardiac muscle contraction due to inhibition of the  $\text{Na}^+/\text{K}^+$ ATPase pump

### Digoxin toxicity

Plasma concentration alone does not determine whether a patient has developed digoxin toxicity. The BNF advises that the likelihood of toxicity increases progressively from 1.5 to 3 mcg/l.

Features

- generally unwell, lethargy, nausea & vomiting, anorexia, confusion, yellow-green vision
- arrhythmias (e.g. AV block, bradycardia)

Precipitating factors

- classically: hypokalaemia\*
- increasing age
- renal failure
- myocardial ischaemia
- hypomagnesaemia, hypercalcaemia, hyponatraemia, acidosis
- hypoalbuminaemia



- hypothermia
- hypothyroidism
- drugs: amiodarone, quinidine, verapamil, diltiazem, spironolactone (compete for secretion in distal convoluted tubule therefore reduce excretion). Also drugs which cause hypokalaemia e.g. thiazides and loop diuretics

## Management

- Digibind
- correct arrhythmias
- monitor potassium

\*hyperkalaemia may also worsen digoxin toxicity, although this is very small print

A 65-year-old man with a history of ischaemic heart disease is admitted with chest pain. The 12-hour troponin T is negative. During admission his medications were altered to reduce the risk of cardiovascular disease and to treat previously undiagnosed type 2 diabetes mellitus. Shortly after discharge he presents to his GP complaining of diarrhoea. Which one of the following medications is most likely to be responsible?

- |                                  |                  |
|----------------------------------|------------------|
| <input type="radio"/>            | A. Gliclazide    |
| <input type="radio"/>            | B. Clopidogrel   |
| <input type="radio"/>            | C. Rosiglitazone |
| <input checked="" type="radio"/> | D. Metformin     |
| <input type="radio"/>            | E. Atorvastatin  |

[Next question](#)

Gastrointestinal problems are a common side-effect of many medications but are frequently seen in patients taking metformin

If this patient had a raised troponin T then metformin may not be suitable as it is contraindicated following recent episodes of tissue hypoxia.

### Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

#### Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

#### Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis\* with severe liver disease or renal failure

#### Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is  $> 130 \mu\text{mol/l}$  and stopping metformin if  $> 150 \mu\text{mol/l}$

- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication
- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

Which one of the following statements regarding drug metabolism is incorrect?

<input type="radio"/>	A. Reduction is an example of a phase I reaction
<input type="radio"/>	B. The majority of both phase I and phase II reactions take place in the liver
<input type="radio"/>	C. Aspirin undergoes extensive first-pass metabolism
<input type="radio"/>	D. Products of phase I reactions are typically more lipid soluble
<input type="radio"/>	E. Products of phase II reactions are typically inactive and excreted in urine or bile

Next question

Usually both phase I and II reactions decrease lipid solubility

### Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

### First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are needed orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil
- isoprenaline
- testosterone
- hydrocortisone

Questions concerning zero-order kinetics and acetylator status are also common in the exam

## **Zero-order kinetics**

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

## **Acetylator status**

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

A 61-year-old female is reviewed in the rheumatology clinic with increasing shortness of breath. She has been on long-term drug therapy to control her rheumatoid arthritis and has a 40 pack-year history of smoking. Her oxygen saturations on room air are on 89%. Investigations reveal the following:

FEV1%	80%
Transfer factor coefficient (TLCO)	41%

What is the most likely cause for her symptoms?

- ☐ A. Pulmonary nodules
- ☐ B. Methotrexate pneumonitis
- ☐ C. Pulmonary haemorrhage
- ☐ D. Bronchiolitis obliterans
- ☐ E. Chronic obstructive pulmonary disease

Next question

A FEV1% of 80% would not support a diagnosis of COPD or bronchiolitis obliterans. Methotrexate pneumonitis is potentially life-threatening and occurs in 1-5% of patients who are treated with methotrexate. Pulmonary fibrosis should be part of the differential diagnosis

### Rheumatoid arthritis: respiratory manifestations

A variety of respiratory problems may be seen in patients with rheumatoid arthritis:

- pulmonary fibrosis
- pleural effusion
- pulmonary nodules
- bronchiolitis obliterans
- complications of drug therapy e.g. methotrexate pneumonitis
- pleurisy
- Caplan's syndrome - massive fibrotic nodules with occupational coal dust exposure
- infection (possibly atypical) secondary to immunosuppression

A 41-year-old alcoholic is admitted with a suspected variceal haemorrhage. Terlipressin is given. What is the main mechanism of action of terlipressin?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Portal system vasodilation             |
| <input type="radio"/> | B. Antifibrinolytic                       |
| <input type="radio"/> | C. Constriction of hepatic venules        |
| <input type="radio"/> | D. Endothelin-1 antagonist                |
| <input type="radio"/> | E. Constriction of the splanchnic vessels |

[Next question](#)

Terlipressin - method of action = constriction of the splanchnic vessels

## Oesophageal varices

### Acute treatment of variceal haemorrhage

- ABC: patients should ideally be resuscitated prior to endoscopy
- correct clotting: FFP, vitamin K
- vasoactive agents: terlipressin is currently the only licensed vasoactive agent and is supported by NICE guidelines. It has been shown to be of benefit in initial haemostasis and preventing rebleeding. Octreotide may also be used although there is some evidence that terlipressin has a greater effect on reducing mortality
- prophylactic antibiotics have been shown in multiple meta-analyses to reduce mortality in patients with liver cirrhosis
- endoscopy: endoscopic variceal band ligation is superior to endoscopic sclerotherapy. NICE recommend band ligation
- Sengstaken-Blakemore tube if uncontrolled haemorrhage
- Transjugular Intrahepatic Portosystemic Shunt (TIPSS) if above measures fail

### Prophylaxis of variceal haemorrhage

- propranolol: reduced rebleeding and mortality compared to placebo
- endoscopic variceal band ligation (EVL) is superior to endoscopic sclerotherapy. It should be performed at two-weekly intervals until all varices have been eradicated. Proton pump inhibitor cover is given to prevent EVL-induced ulceration

What is the mode of action of bisphosphonates?

- |                                  |                                 |
|----------------------------------|---------------------------------|
| <input type="radio"/>            | A. Promotes osteoblasts         |
| <input type="radio"/>            | B. Promotes calcium absorption  |
| <input type="radio"/>            | C. Antagonist of PTH            |
| <input checked="" type="radio"/> | D. Inhibit osteoclasts          |
| <input type="radio"/>            | E. Promotes phosphate excretion |

Next question

Bisphosphonates inhibit osteoclasts

## Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

### Clinical uses

- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metastases

### Adverse effects

- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw
- increased risk of atypical stress fractures of the proximal femoral shaft in patients taking alendronate

The BNF suggests the following counselling for patients taking oral bisphosphonates

- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'



A 36-year-old former intravenous drug user is to commence treatment for hepatitis C with interferon-alpha and ribavirin. Which of the following adverse effects are most likely to occur when patients are treated with interferon-alpha?

<input type="radio"/>	A. Diarrhoea and transient rise in ALT
<input type="radio"/>	B. Cough and haemolytic anaemia
<input type="radio"/>	C. Flu-like symptoms and transient rise in ALT
<input type="radio"/>	D. Haemolytic anaemia and flu-like symptoms
<input type="radio"/>	E. Depression and flu-like symptoms

[Next question](#)

## Interferon

Interferons (IFN) are cytokines released by the body in response to viral infections and neoplasia. They are classified according to cellular origin and the type of receptor they bind to. IFN-alpha and IFN-beta bind to type 1 receptors whilst IFN-gamma binds only to type 2 receptors.

### IFN-alpha

- produced by leucocytes
- antiviral action
- useful in hepatitis B & C, Kaposi's sarcoma, metastatic renal cell cancer, hairy cell leukaemia
- adverse effects include flu-like symptoms and depression

### IFN-beta

- produced by fibroblasts
- antiviral action
- reduces the frequency of exacerbations in patients with relapsing-remitting MS

### IFN-gamma

- produced by T lymphocytes & NK cells
- weaker antiviral action, more of a role in immunomodulation particularly macrophage activation
- may be useful in chronic granulomatous disease and osteopetrosis

A 44-year-old man asks for advice. He is due to go on a long bus journey but suffers from debilitating motion sickness. Which one of the following medications is most likely to prevent motion sickness?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Cyclizine        |
| <input type="radio"/> | B. Chlorpromazine   |
| <input type="radio"/> | C. Metoclopramide   |
| <input type="radio"/> | D. Prochlorperazine |
| <input type="radio"/> | E. Domperidone      |

[Next question](#)

Motion sickness - hyoscine > cyclizine > promethazine

### Motion sickness

Motion sickness describes the nausea and vomiting which occurs when an apparent discrepancy exists between visually perceived movement and the vestibular systems sense of movement

#### Management

- the BNF recommends hyoscine (e.g. transdermal patch) as being the most effective treatment. Use is limited due to side-effects
- non-sedating antihistamines such as cyclizine or cinnarizine are recommended in preference to sedating preparation such as promethazine

What is the mechanism of action of ciclosporin?

<input type="radio"/>	A. Monoclonal antibody against IL-2 receptor
<input type="radio"/>	B. Interferes with purine synthesis
<input type="radio"/>	C. Inhibits inosine monophosphate dehydrogenase
<input checked="" type="radio"/>	D. Decreases IL-2 release by inhibiting calcineurin
<input type="radio"/>	E. Mercaptopurine antagonist

Next question

Ciclosporin - decreases IL-2 release by inhibiting calcineurin

### Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphatase that activates various transcription factors in T cells

Adverse effects of ciclosporin (note how everything is increased - fluid, BP, K<sup>+</sup>, hair, gums, glucose)

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- gingival hyperplasia
- tremor
- impaired glucose tolerance

Interestingly for an immunosuppressant, ciclosporin is noted by the BNF to be 'virtually non-myelotoxic'.

### Indications

- following organ transplantation
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- ulcerative colitis
- pure red cell aplasia

What is the mechanism of action of sumatriptan?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. 5-HT <sub>3</sub> agonist    |
| <input type="radio"/> | B. 5-HT <sub>2</sub> antagonist |
| <input type="radio"/> | C. 5-HT <sub>2</sub> agonist    |
| <input type="radio"/> | D. 5-HT <sub>1</sub> antagonist |
| <input type="radio"/> | E. 5-HT <sub>1</sub> agonist    |

Next question

Triptans are specific agonists of 5-HT<sub>1B/1D</sub> receptors.

### Triptans

Triptans are specific 5-HT<sub>1</sub> agonists used in the acute treatment of migraine. They are generally used first-line in combination therapy with an NSAID or paracetamol.

#### Prescribing points

- should be taken as soon as possible after the onset of headache, rather than at onset of aura
- oral, orodispersible, nasal spray and subcutaneous injections are available

#### Adverse effects

- 'triptan sensations' - tingling, heat, tightness (e.g. throat and chest), heaviness, pressure

#### Contraindications

- patients with a history of, or significant risk factors for, ischaemic heart disease or cerebrovascular disease

A 19-year-old man presents to the Emergency Department 5 hours ingesting 20g of paracetamol. N-acetyl cysteine is started straight away. What is the mechanism of action of N-acetyl cysteine?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Replenishes glutathione                             |
| <input type="radio"/> | B. Inhibits P450 mixed function oxidases               |
| <input type="radio"/> | C. Replenishes glucuronic acid                         |
| <input type="radio"/> | D. Promotes formation of N-acetyl-B-benzoquinone imine |
| <input type="radio"/> | E. Neutralises mercapturic acid                        |

[Next question](#)

### Paracetamol overdose: metabolic pathways

The liver normally conjugates paracetamol with glucuronic acid/sulphate. During an overdose the conjugation system becomes saturated leading to oxidation by P450 mixed function oxidases\*. This produces a toxic metabolite (N-acetyl-B-benzoquinone imine)

Normally glutathione acts as a defence mechanism by conjugating with the toxin forming the non-toxic mercapturic acid. If glutathione stores run-out, the toxin forms covalent bonds with cell proteins, denaturing them and leading to cell death. This occurs not only in hepatocytes but also in the renal tubules

N-acetyl cysteine is used in the management of paracetamol overdose as it is a precursor of glutathione and hence can increase hepatic glutathione production

\*this explains why there is a lower threshold for treating patients who take P450 inducing medications e.g. phenytoin or rifampicin

Which of the following drugs is considered least likely to precipitate an attack of acute intermittent porphyria?

<input type="radio"/>	A. Diazepam
<input type="radio"/>	B. Penicillin
<input type="radio"/>	C. Thiopentone
<input type="radio"/>	D. Sulphonamides
<input type="radio"/>	E. Alcohol

Next question

### Acute intermittent porphyria: drugs

Acute intermittent porphyria (AIP) is an autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40 year olds. AIP is more common in females (5:1)

Drugs which may precipitate attack

- barbiturates
- halothane
- benzodiazepines
- alcohol
- oral contraceptive pill
- sulphonamides

Drugs considered safe to use

- paracetamol
- aspirin
- codeine
- morphine
- chlorpromazine
- beta-blockers
- penicillin
- metformin

Which one of the following drugs is contra-indicated whilst breast feeding?

<input type="radio"/>	A. Aminophylline
<input type="radio"/>	B. Carbamazepine
<input type="radio"/>	C. Sodium valproate
<input type="radio"/>	D. Methyldopa
<input type="radio"/>	E. Amiodarone

### Breast feeding: contraindications

The major breastfeeding contraindications tested in exams relate to drugs (see below). Other contraindications of note include:

- galactosaemia
- viral infections - this is controversial with respect to HIV in the developing world. This is because there is such an increased infant mortality and morbidity associated with bottle feeding that some doctors think the benefits outweigh the risk of HIV transmission

### Drug contraindications

The following drugs can be given to mothers who are breast feeding:

- antibiotics: penicillins, cephalosporins, trimethoprim
- endocrine: glucocorticoids (avoid high doses), levothyroxine\*
- epilepsy: sodium valproate, carbamazepine
- asthma: salbutamol, theophyllines
- psychiatric drugs: tricyclic antidepressants, antipsychotics\*\*
- hypertension: beta-blockers, hydralazine, methyldopa
- anticoagulants: warfarin, heparin
- digoxin

The following drugs should be avoided:

- antibiotics: ciprofloxacin, tetracycline, chloramphenicol, sulphonamides
- psychiatric drugs: lithium, benzodiazepines
- aspirin
- carbimazole
- sulphonylureas
- cytotoxic drugs
- amiodarone

\*the BNF advises that the amount is too small to affect neonatal hypothyroidism screening

\*\*clozapine should be avoided

A 31-year-old female with a history of epilepsy consults you following an uneventful pregnancy. Which one of the following drugs would it be safe to continue during breast feeding?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Phenytoin        |
| <input type="radio"/> | B. Carbamazepine    |
| <input type="radio"/> | C. Lamotrigine      |
| <input type="radio"/> | D. Sodium valproate |
| <input type="radio"/> | E. All of the above |

[Next question](#)

Breast feeding is acceptable with nearly all anti-epileptic drugs

The BNF states 'breast-feeding is acceptable with all antiepileptic drugs, taken in normal doses, with the possible exception of barbiturates'

### Epilepsy: pregnancy and breast feeding

The risks of uncontrolled epilepsy during pregnancy generally outweigh the risks of medication to the fetus. All women thinking about becoming pregnant should be advised to take folic acid 5mg per day well before pregnancy to minimise the risk of neural tube defects. Around 1-2% of newborns born to non-epileptic mothers have congenital defects. This rises to 3-4% if the mother takes antiepileptic medication.

#### Other points

- aim for monotherapy
- there is no indication to monitor antiepileptic drug levels
- sodium valproate: associated with neural tube defects
- carbamazepine: often considered the least teratogenic of the older antiepileptics
- phenytoin: associated with cleft palate
- lamotrigine: studies to date suggest the rate of congenital malformations may be low. The dose of lamotrigine may need to be increased in pregnancy

Breast feeding is generally considered safe for mothers taking antiepileptics with the possible exception of the barbiturates

It is advised that pregnant women taking phenytoin are given vitamin K in the last month of pregnancy to prevent clotting disorders in the newborn



**Question 171 of 265**

Next

A 47-year-old female is reviewed in the neurology clinic. She was diagnosed with epilepsy whilst a teenager and her seizures are well controlled. She is however concerned about increasing numbness of her fingers and soles of her feet. Which one of the following medications is most likely to be responsible?

<input type="radio"/>	A. Phenytoin
<input type="radio"/>	B. Lamotrigine
<input type="radio"/>	C. Sodium valproate
<input type="radio"/>	D. Ethosuximide
<input type="radio"/>	E. Levetiracetam

Next question

Peripheral neuropathy is a known adverse effect of phenytoin

**Phenytoin**

Phenytoin is used to in the management of seizures.

Mechanism of action

- sodium channel blocker, decreasing the sodium influx into neurons which in turn decreases excitability

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute

- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic

- common: gingival hyperplasia (secondary to increased expression of platelet derived growth factor, PDGF), hirsutism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

Idiosyncratic

- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture\*
- aplastic anaemia
- drug-induced lupus

#### Teratogenic

- associated with cleft palate and congenital heart disease

\*although not listed in the BNF

Which of the following conditions may not be treated by dopamine receptor agonists?

<input type="radio"/>	A. Parkinson's disease
<input type="radio"/>	B. Prolactinoma
<input type="radio"/>	C. Nausea
<input type="radio"/>	D. Cyclical breast disease
<input type="radio"/>	E. Acromegaly

### Dopamine receptor agonists

#### Indications

- Parkinson's disease
- prolactinoma/galactorrhoea
- cyclical breast disease
- acromegaly

Currently accepted practice in the management of patients with Parkinson's disease is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, L-dopa is sometimes used as an initial treatment

#### Overview

- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

#### Adverse effects

- nausea/vomiting
- postural hypotension
- hallucinations
- daytime somnolence

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

### Question 173 of 265

Which one of the following unwanted effects is most likely to occur in patients taking gliclazide?

<input type="radio"/>	A. Peripheral neuropathy
<input type="radio"/>	B. Cholestasis
<input type="radio"/>	C. Photosensitivity
<input type="radio"/>	D. Syndrome of inappropriate ADH secretion
<input type="radio"/>	E. Weight gain

[Next question](#)

All of the above side-effects may be seen in patients taking sulfonylureas but weight gain is the most common.

### Sulfonylureas

Sulfonylureas are oral hypoglycaemic drugs used in the management of type 2 diabetes mellitus. They work by increasing pancreatic insulin secretion and hence are only effective if functional B-cells are present.

#### Common adverse effects

- hypoglycaemic episodes (more common with long acting preparations such as chlorpropamide)
- weight gain

#### Rarer adverse effects

- syndrome of inappropriate ADH secretion
- bone marrow suppression
- liver damage (cholestatic)
- photosensitivity
- peripheral neuropathy

Sulfonylureas should be avoided in breast feeding and pregnancy

A 62-year-old man presents four weeks after initiating metformin for type 2 diabetes mellitus. His body mass index is 27.5 kg/m<sup>2</sup>. Despite slowly titrating the dose up to 500mg tds he has experienced significant diarrhoea. He has tried reducing the dose back down to 500mg bd but his symptoms persisted. What is the most appropriate action?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Switch to pioglitazone 15mg od                              |
| <input type="radio"/> | B. Switch to gliclazide 40mg od                                |
| <input type="radio"/> | C. Start modified release metformin 500mg od with evening meal |
| <input type="radio"/> | D. Add loperamide as required                                  |
| <input type="radio"/> | E. Arrange colonoscopy   |

[Next question](#)

If a patient is intolerant to standard metformin then modified-release preparations should be tried. There is some evidence that these produce fewer gastrointestinal side-effects in patients intolerant of standard-release metformin.

### Metformin

Metformin is a biguanide used mainly in the treatment of type 2 diabetes mellitus. It has a number of actions which improves glucose tolerance (see below). Unlike sulphonylureas it does not cause hypoglycaemia and weight gain and is therefore first-line, particularly if the patient is overweight. Metformin is also used in polycystic ovarian syndrome and non-alcoholic fatty liver disease

#### Mechanism of action

- increases insulin sensitivity
- decreases hepatic gluconeogenesis
- may also reduce gastrointestinal absorption of carbohydrates

#### Adverse effects

- gastrointestinal upsets are common (nausea, anorexia, diarrhoea), intolerable in 20%
- reduced vitamin B12 absorption - rarely a clinical problem
- lactic acidosis\* with severe liver disease or renal failure

#### Contraindications\*\*

- chronic kidney disease: NICE recommend reviewing metformin if the creatinine is > 130 µmol/l and stopping metformin if > 150 µmol/l
- do not use during suspected episodes of tissue hypoxia (e.g. Recent MI, sepsis)
- alcohol abuse is a relative contraindication

- stop 2 days before general anaesthetic, restart when renal function normal
- stop prior to IV contrast e.g. Angiography, restart when renal function normal

\*it is now increasingly recognised that lactic acidosis secondary to metformin is rare, although it remains important in the context of exams

\*\*metformin is now sometimes used in pregnancy, for example in women with polycystic ovarian syndrome

A 46-year-old man is admitted to hospital with chest pain. An ECG shows an anterior ST elevation myocardial infarction and he receives thrombolysis. His past medical history includes hypertension and he drinks around 70 units of alcohol per week. Three days following admission he becomes confused. What treatment is most likely to help?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Benzodiazepines        |
| <input type="radio"/> | B. Thiamine               |
| <input type="radio"/> | C. Frusemide              |
| <input type="radio"/> | D. Renal angioplasty      |
| <input type="radio"/> | E. Neurosurgical referral |

[Next question](#)

The most likely cause for confusion in this man is alcohol withdrawal which should be treated with benzodiazepines in the acute phase. Wernicke's encephalopathy can cause confusion, but questions would normally hint at more classical features such as ataxia, ophthalmoplegia or nystagmus. Also, if there were focal signs or failure to improve with benzodiazepines then a CT scan should be performed to exclude a subdural, given that he has a history of alcohol excess and has been thrombolysed

### Alcohol withdrawal

#### Mechanism

- chronic alcohol consumption enhances GABA mediated inhibition in the CNS (similar to benzodiazepines) and inhibits NMDA-type glutamate receptors
- alcohol withdrawal is thought to lead to the opposite (decreased inhibitory GABA and increased NMDA glutamate transmission)

#### Features

- symptoms start at 6-12 hours
- peak incidence of seizures at 36 hours
- peak incidence of delirium tremens is at 72 hours

#### Management

- benzodiazepines
- carbamazepine also effective in treatment of alcohol withdrawal
- phenytoin is said not to be as effective in the treatment of alcohol withdrawal seizures

A 22-year-old man consults you as he and his housemate have been feeling generally unwell for the past few weeks. Which one of the following is the most common feature of carbon monoxide poisoning?

<input type="radio"/>	A. Hyperpyrexia
<input type="radio"/>	B. Nausea
<input type="radio"/>	C. Cherry red skin
<input type="radio"/>	D. Confusion
<input type="radio"/>	E. Headache

[Next question](#)

Carbon monoxide poisoning - most common feature = headache

Cherry red skin is a sign of severe toxicity and is usually seen post-mortem

### Carbon monoxide poisoning

Carbon monoxide has high affinity for haemoglobin and myoglobin resulting in a left-shift of the oxygen dissociation curve and tissue hypoxia. There are approximately 50 per year deaths from accidental carbon monoxide poisoning in the UK

Questions may hint at badly maintained housing e.g. student houses

Features of carbon monoxide toxicity

- headache: 90% of cases
- nausea and vomiting: 50%
- vertigo: 50%
- confusion: 30%
- subjective weakness: 20%
- severe toxicity: 'pink' skin and mucosae, hyperpyrexia, arrhythmias, extrapyramidal features, coma, death

Typical carboxyhaemoglobin levels

- < 3% non-smokers
- < 10% smokers
- 10 - 30% symptomatic: headache, vomiting
- > 30% severe toxicity

Management



- 100% oxygen
- hyperbaric oxygen

Indications for hyperbaric oxygen\*

- loss of consciousness at any point
- neurological signs other than headache
- myocardial ischaemia or arrhythmia
- pregnancy

\*as stated in the 2008 Department of Health publication 'Recognising Carbon Monoxide Poisoning'

A 61-year-old man with peripheral arterial disease is prescribed simvastatin. What is the most appropriate blood test monitoring?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. LFTs + creatinine kinase at baseline, 1-3 months and at intervals of 6 months for 1 year |
| <input type="radio"/> | B. LFTs at baseline and every 3 months for first year                                       |
| <input type="radio"/> | C. Routine blood tests not recommended  |
| <input type="radio"/> | D. LFTs at baseline and annually  |
| <input type="radio"/> | E. LFTs at baseline, 3 months and 12 months   |

Next question

A fasting lipid profile may also be checked during monitoring to assess response to treatment.

## Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

### Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

### Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk  $\geq 20\%$
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering\*

	Total cholesterol (mmol/l)	LDL cholesterol
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

\*current NICE guidelines do not recommend a target cholesterol in primary prevention

Which one of the following side-effects is least recognised in patients taking isotretinoin?

<input type="radio"/>	A. Hypertension
<input type="radio"/>	B. Teratogenicity
<input type="radio"/>	C. Nose bleeds
<input type="radio"/>	D. Depression
<input type="radio"/>	E. Raised triglycerides

Next question

#### Isotretinoin adverse effects

- teratogenicity - females **MUST** be taking contraception
- low mood
- dry eyes and lips
- raised triglycerides
- hair thinning
- nose bleeds

Hypertension is not listed in the British National Formulary as a side-effect

#### Isotretinoin

Isotretinoin is an oral retinoid used in the treatment of severe acne. Two-thirds of patients have a long term remission or cure following a course of oral isotretinoin

#### Adverse effects

- teratogenicity: females should ideally be using two forms of contraception (e.g. Combined oral contraceptive pill and condoms)
- dry skin, eyes and lips: the most common side-effect of isotretinoin
- low mood
- raised triglycerides
- hair thinning
- nose bleeds (caused by dryness of the nasal mucosa)
- benign intracranial hypertension: isotretinoin treatment should not be combined with tetracyclines for this reason

Which one of the following statements regarding raloxifene in the management of osteoporosis is incorrect?

<input type="radio"/>	A.	Has been shown to prevent bone loss and to reduce the risk of vertebral fractures
<input type="radio"/>	B.	Is a selective oestrogen receptor modulator
<input type="radio"/>	C.	May worsen menopausal symptoms
<input type="radio"/>	D.	Increases risk of thromboembolic events
<input type="radio"/>	E.	Increases the risk of breast cancer

Next question

Raloxifene may actually decrease the risk of breast cancer

### Osteoporosis: secondary prevention

NICE guidelines were updated in 2008 on the secondary prevention of osteoporotic fractures in postmenopausal women.

Key points include

- treatment is indicated following osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (a T-score of - 2.5 SD or below). In women aged 75 years or older, a DEXA scan may not be required 'if the responsible clinician considers it to be clinically inappropriate or unfeasible'
- vitamin D and calcium supplementation should be offered to all women unless the clinician is confident they have adequate calcium intake and are vitamin D replete
- alendronate is first-line
- around 25% of patients cannot tolerate alendronate, usually due to upper gastrointestinal problems. These patients should be offered risedronate or etidronate (see treatment criteria below)
- strontium ranelate and raloxifene are recommended if patients cannot tolerate bisphosphonates (see treatment criteria below)

### Treatment criteria for patients not taking alendronate

Unfortunately, a number of complicated treatment cut-off tables have been produced in the latest guidelines for patients who do not tolerate alendronate

Risk factors (for use in the tables below)

- parental history of hip fracture
- alcohol intake of 4 or more units per day
- rheumatoid arthritis

T-scores (SD) at (or below) which risedronate or etidronate is recommended when alendronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50-54	Not indicated	- 3.0	- 2.5
55-59	- 3.0	- 3.0	- 2.5
60-64	- 3.0	- 3.0	- 2.5
65-69	- 3.0	- 2.5	- 2.5
70 or older	- 2.5	- 2.5	- 2.5

T-scores (SD) at (or below) which strontium ranelate or raloxifene is recommended when alendronate and either risedronate or etidronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50-54	Not indicated	- 3.5	- 3.5
55-59	- 4.0	- 3.5	- 3.5
60-64	- 4.0	- 3.5	- 3.5
65-69	- 4.0	- 3.5	- 3.0
70-74	- 3.0	- 3.0	- 2.5
75 or older	- 3.0	- 2.5	- 2.5

## Supplementary notes on treatment

### Bisphosphonates

- alendronate, risedronate and etidronate are all licensed for the prevention and treatment of post-menopausal and glucocorticoid-induced osteoporosis
- all three have been shown to reduce the risk of both vertebral and non-vertebral fractures although alendronate, risedronate may be superior to etidronate in preventing hip fractures
- ibandronate is a once-monthly oral bisphosphonate

### Vitamin D and calcium

- poor evidence base to suggest reduced fracture rates in the general population at risk of osteoporotic fractures - may reduce rates in frail, housebound patients

## Raloxifene - selective oestrogen receptor modulator (SERM)

- has been shown to prevent bone loss and to reduce the risk of vertebral fractures, but has not yet been shown to reduce the risk of non-vertebral fractures
- has been shown to increase bone density in the spine and proximal femur
- may worsen menopausal symptoms
- increased risk of thromboembolic events
- may decrease risk of breast cancer

## Strontium ranelate

- 'dual action bone agent' - increases deposition of new bone by osteoblasts and reduces the resorption of bone by osteoclasts
- strong evidence base, may be second-line treatment in near future
- increased risk of thromboembolic events

## Teriparatide

- recombinant form of parathyroid hormone
- very effective at increasing bone mineral density but role in the management of osteoporosis yet to be clearly defined

## Hormone replacement therapy

- has been shown to reduce the incidence of vertebral fracture and non-vertebral fractures
- due to concerns about increased rates of cardiovascular disease and breast cancer it is no longer recommended for primary or secondary prevention of osteoporosis unless the woman is suffering from vasomotor symptoms

## Hip protectors

- evidence to suggest significantly reduce hip fractures in nursing home patients
- compliance is a problem

## Falls risk assessment

- no evidence to suggest reduced fracture rates
- however, do reduce rate of falls and should be considered in management of high risk patients

A 55-year-old man who has a history of ischaemic heart disease presents with myalgia. His long-term medications include aspirin, simvastatin and atenolol. Given his statin use a creatine kinase is measured and reported as follows:

Creatine kinase	1,420 u/l (< 190 u/l)
-----------------	-----------------------

His problems seem to have followed the prescription of a new medication. Which one of the following is most likely to have caused the elevation in creatine kinase?

- ☐ A. Rifampicin
- ☐ B. Felodipine
- ☐ C. Clarithromycin
- ☐ D. Ciprofloxacin
- ☐ E. Amitriptyline

Next question

Statins + erythromycin/clarithromycin - an important and common interaction

This patient has developed statin-induced myopathy secondary to clarithromycin, which is a known inhibitor of the CYP3A4 enzyme system.

## Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

### Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

### Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk  $\geq 20\%$



- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering\*

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SIGN 2007	< 5.0	< 3.0

\*current NICE guidelines do not recommend a target cholesterol in primary prevention

A 76-year-old woman is diagnosed with Alzheimer's disease. Which one of the following could be a contraindication to the prescription of donepezil?

<input type="radio"/>	A. History of depression
<input type="radio"/>	B. Sick sinus syndrome
<input type="radio"/>	C. Concurrent simvastatin therapy
<input type="radio"/>	D. Concurrent citalopram therapy
<input type="radio"/>	E. Ischaemic heart disease

Donepezil may cause bradycardia and atrioventricular node block.

### Alzheimer's disease

Alzheimer's disease is a progressive degenerative disease of the brain accounting for the majority of dementia seen in the UK

#### Genetics

- most cases are sporadic
- 5% of cases are inherited as an autosomal dominant trait
- mutations in the amyloid precursor protein (chromosome 21), presenilin 1 (chromosome 14) and presenilin 2 (chromosome 1) genes are thought to cause the inherited form
- apoprotein E allele E4 - encodes a cholesterol transport protein

#### Pathological changes

- macroscopic = widespread cerebral atrophy, particularly involving the cortex and hippocampus
- microscopic = intraneuronal neurofibrillary tangles, neuronal plaques, deficiency of neurons
- biochemical = deposition of type A-Beta-amyloid protein in cortex, deficit of Ach from damage to an ascending forebrain projection

#### Neurofibrillary tangles

- paired helical filaments are partly made from a protein called tau
- in AD tau proteins are excessively phosphorylated

#### Management

- NICE now recommend the three acetylcholinesterase inhibitors (donepezil, galantamine and rivastigmine) as options for managing mild to moderate Alzheimer's disease
- memantine is reserved for patients with moderate - severe Alzheimer's

What is the mechanism of action of nicorandil?

<input type="radio"/>	A. Fast-sodium channel antagonist
<input type="radio"/>	B. Nitric oxide reductase inhibitor
<input type="radio"/>	C. Acts on the $I_f$ ion current in the sinoatrial node
<input type="radio"/>	D. Potassium-channel activator
<input type="radio"/>	E. Glutathione S-transferase inhibitor

Next question

### Angina pectoris: drug management

The management of stable angina comprises lifestyle changes, medication, percutaneous coronary intervention and surgery. NICE produced guidelines in 2011 covering the management of stable angina

#### Medication

- all patients should receive aspirin and a statin in the absence of any contraindication
- sublingual glyceryl trinitrate to abort angina attacks
- NICE recommend using either a beta-blocker or a calcium channel blocker first-line based on 'comorbidities, contraindications and the person's preference'
- if a calcium channel blocker is used as monotherapy a rate-limiting one such as verapamil or diltiazem should be used. If used in combination with a beta-blocker then use a long-acting dihydropyridine calcium-channel blocker (e.g. modified-release nifedipine). Remember that beta-blockers should not be prescribed concurrently with verapamil (risk of complete heart block)
- if there is a poor response to initial treatment then medication should be increased to the maximum tolerated dose (e.g. for atenolol 100mg od)
- if a patient is still symptomatic after monotherapy with a beta-blocker add a calcium channel blocker and vice versa
- if a patient is on monotherapy and cannot tolerate the addition of a calcium channel blocker or a beta-blocker then consider one of the following drugs: a long-acting nitrate, ivabradine, nicorandil or ranolazine
- if a patient is taking both a beta-blocker and a calcium-channel blocker then only add a third drug whilst a patient is awaiting assessment for PCI or CABG

#### Nitrate tolerance

- many patients who take nitrates develop tolerance and experience reduced efficacy
- the BNF advises that patients who develop tolerance should take the second dose of isosorbide mononitrate after 8 hours, rather than after 12 hours. This allows blood-nitrate levels to fall for 4 hours and maintains effectiveness
- this effect is not seen in patients who take modified release isosorbide mononitrate

## Ivabradine

- a new class of anti-anginal drug which works by reducing the heart rate
- acts on the  $I_f$  ('funny') ion current which is highly expressed in the sinoatrial node, reducing cardiac pacemaker activity
- adverse effects: visual effects, particular luminous phenomena, are common. Bradycardia, due to the mechanism of action, may also be seen
- there is no evidence currently of superiority over existing treatments of stable angina

Which of the following drugs is least likely to cause cholestasis?

<input type="radio"/>	A. Gliclazide
<input type="radio"/>	B. Amiodarone
<input type="radio"/>	C. Chlorpromazine
<input type="radio"/>	D. Oral contraceptive pill
<input type="radio"/>	E. Co-amoxiclav

### Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin\*, nitrofurantoin
- anabolic steroids, testosterone
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

\*risk may be reduced with erythromycin stearate

A 34-year-old man who is known to have glucose-6-phosphate dehydrogenase deficiency presents with symptoms of a urinary tract infection. He is prescribed an antibiotic. A few days later he becomes unwell and is noticed by his partner to be pale and jaundiced. What drug is mostly likely to have been prescribed?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Co-amoxiclav  |
| <input type="radio"/> | B. Trimethoprim  |
| <input type="radio"/> | C. Ciprofloxacin |
| <input type="radio"/> | D. Cefalexin     |
| <input type="radio"/> | E. Erythromycin  |

Next question

The sulfamethoxazole in co-trimoxazole causes haemolysis in G6PD, not the trimethoprim

### G6PD deficiency

Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the commonest red blood cell enzyme defect. It is more common in people from the Mediterranean and Africa and is inherited in a X-linked recessive fashion. Many drugs can precipitate a crisis as well as infections and broad (fava) beans

#### Features

- neonatal jaundice is often seen
- intravascular haemolysis
- Heinz bodies on blood films

Diagnosis is made by using a G6PD enzyme assay

#### Some drugs causing haemolysis

- anti-malarials: primaquine
- ciprofloxacin
- sulphonamides

#### Some drugs thought to be safe

- penicillins
- cephalosporins
- macrolides
- tetracyclines
- trimethoprim

Low molecular weight heparin has the greatest inhibitory effect on which one of the following proteins involved in the coagulation cascade?

- ☐ A. Factor IXa
- ☐ B. Factor XIa
- ☐ C. Factor Xa
- ☐ D. Thrombin
- ☐ E. Factor XIIa

### Heparin

There are two main types of heparin - unfractionated, 'standard' heparin or low molecular weight heparin (LMWH). Heparins generally act by activating antithrombin III. Unfractionated heparin forms a complex which inhibits thrombin, factors Xa, IXa, XIa and XIIa. LMWH however only increases the action of antithrombin III on factor Xa

The table below shows the differences between standard heparin and LMWH:

	Standard heparin	Low molecular weight heparin (LMWH)
<b>Administration</b>	Intravenous	Subcutaneous
<b>Duration of action</b>	Short	Long
<b>Mechanism of action</b>	Activates antithrombin III. Forms a complex that inhibits thrombin, factors Xa, IXa, XIa and XIIa	Activates antithrombin III. Forms a complex that inhibits factor Xa
<b>Side-effects</b>	Bleeding Heparin-induced thrombocytopenia (HIT) Osteoporosis	Bleeding  Lower risk of HIT and osteoporosis with LMWH
<b>Monitoring</b>	Activated partial thromboplastin time (APTT)	Anti-Factor Xa (although routine monitoring is not required)
<b>Notes</b>	Useful in situations where there is a high risk of bleeding as anticoagulation can be terminated rapidly	Now standard in the management of venous thromboembolism treatment and prophylaxis and acute coronary syndromes

## Heparin-induced thrombocytopenia (HIT)

- immune mediated - antibodies form which cause the activation of platelets
- usually does not develop until after 5-10 days of treatment
- despite being associated with low platelets HIT is actually a prothrombotic condition
- features include a greater than 50% reduction in platelets, thrombosis and skin allergy
- treatment options include alternative anticoagulants such as lepirudin and danaparoid

Both unfractionated and low-molecular weight heparin can cause hyperkalaemia. This is thought to be caused by inhibition of aldosterone secretion.

Heparin overdose may be reversed by protamine sulphate, although this only partially reverses the effect of LMWH.



Which one of the following statements regarding amiodarone-induced thyrotoxicosis (AIT) is correct?

- ☐ A. AIT type 2 should be treated with corticosteroids
- ☐ B. Amiodarone should be continued in the majority of patients
- ☐ C. Carbimazole is contraindicated in AIT type 1
- ☐ D. Goitre is usually present in AIT type 2
- ☐ E. AIT type 1 is due to a amiodarone-related destructive thyroiditis

Next question

### Amiodarone and the thyroid gland

Around 1 in 6 patients taking amiodarone develop thyroid dysfunction

#### Amiodarone-induced hypothyroidism

The pathophysiology of amiodarone-induced hypothyroidism (AIH) is thought to be due to the high iodine content of amiodarone causing a Wolff-Chaikoff effect\*

Amiodarone may be continued if this is desirable

#### Amiodarone-induced thyrotoxicosis

Amiodarone-induced thyrotoxicosis (AIT) may be divided into two types:

	AIT type 1	AIT type 2
Pathophysiology	Excess iodine-induced thyroid hormone synthesis	Amiodarone-related destructive thyroiditis
Goitre	Present	Absent
Management	Carbimazole or potassium perchlorate	Corticosteroids

Unlike in AIH, amiodarone should be stopped if possible in patients who develop AIT

\*an autoregulatory phenomenon where thyroxine formation is inhibited due to high levels of circulating iodide

Which one of the following dopamine receptor agonists used in the management of Parkinson's disease is least associated with pulmonary, retroperitoneal and pericardial fibrosis?

<input type="radio"/>	A. Pergolide
<input type="radio"/>	B. Lisuride
<input type="radio"/>	C. Bromocriptine
<input type="radio"/>	D. Cabergoline
<input type="radio"/>	E. Ropinirole

### Parkinson's disease: management

Currently accepted practice in the management of patients with Parkinson's disease (PD) is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, levodopa is sometimes used as an initial treatment.

#### Dopamine receptor agonists

- e.g. Bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an echocardiogram, ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored
- patients should be warned about the potential for dopamine receptor agonists to cause impulse control disorders and excessive daytime somnolence
- nasal congestion and postural hypotension are also seen in some patients

#### Levodopa

- usually combined with a decarboxylase inhibitor (e.g. Carbidopa or benserazide) to prevent peripheral metabolism of levodopa to dopamine
- reduced effectiveness with time (usually by 2 years)
- unwanted effects: dyskinesia (involuntary writhing movements), 'on-off' effect, dry mouth, anorexia, palpitations, postural hypotension, psychosis
- no use in neuroleptic induced parkinsonism

#### MAO-B (Monoamine Oxidase-B) inhibitors

- e.g. Selegiline
- inhibits the breakdown of dopamine secreted by the dopaminergic neurons

## Amantadine

- mechanism is not fully understood, probably increases dopamine release and inhibits its uptake at dopaminergic synapses

## COMT (Catechol-O-Methyl Transferase) inhibitors

- e.g. Entacapone
- COMT is an enzyme involved in the breakdown of dopamine, and hence may be used as an adjunct to levodopa therapy
- used in established PD

## Antimuscarinics

- block cholinergic receptors
- now used more to treat drug-induced parkinsonism rather than idiopathic Parkinson's disease
- help tremor and rigidity
- e.g. Procyclidine, benzotropine, trihexyphenidyl (benzhexol)

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

A 69-year-old man who takes warfarin for atrial fibrillation asks for advice. He is due to have a tooth extraction at the dentist and is unsure what to do with regards to his 'blood-thinning' tablets. There is no other past medical history of note. The last INR was taken two weeks ago and reported as 2.8 with his target INR being 2.0-3.0. What is the most appropriate advice?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Admit to hospital + switch to subcutaneous low-molecular weight heparin prior to extraction |
| <input type="radio"/> | B. Switch to aspirin prior to extraction   |
| <input type="radio"/> | C. Check INR 72 hours before procedure, proceed if INR < 4.0                                   |
| <input type="radio"/> | D. Check INR 72 hours before procedure, proceed if INR < 2.5                                   |
| <input type="radio"/> | E. Admit to hospital + switch to intravenous heparin prior to extraction                       |

[Next question](#)

Dentistry in warfarinised patients - check INR 72 hours before procedure, proceed if INR < 4.0

The BNF gives specific advice with regards to this, in the section 'Prescribing in dental practice'. If a patient has a history of an unstable INR then it should be checked within 24 hours of the dental procedure.

## Warfarin

Warfarin is an oral anticoagulant which inhibits the reduction of vitamin K to its active hydroquinone form, which in turn acts as a cofactor in the formation of clotting factor II, VII, IX and X (mnemonic = 1972) and protein C.

### Indications

- venous thromboembolism: target INR = 2.5, if recurrent 3.5
- atrial fibrillation, target INR = 2.5
- mechanical heart valves, target INR depends on the valve type and location. Mitral valves generally require a higher INR than aortic valves.

Patients on warfarin are monitored using the INR (international normalised ratio), the ratio of the prothrombin time for the patient over the normal prothrombin time. Warfarin has a long half-life and achieving a stable INR may take several days. There a variety of loading regimes and computer software is now often used to alter the dose.

### Factors that may potentiate warfarin

- liver disease
- P450 enzyme inhibitors, e.g.: amiodarone, ciprofloxacin
- cranberry juice

- drugs which displace warfarin from plasma albumin, e.g. NSAIDs
- inhibit platelet function: NSAIDs

#### Side-effects

- haemorrhage
- teratogenic, although can be used in breast-feeding mothers
- skin necrosis: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis
- purple toes

A 34-year-old man with long-standing gastro-oesophageal reflux disease is reviewed in clinic. He has recently switched from ranitidine to omeprazole. What is the main benefit of omeprazole compared to ranitidine?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Increased gastric motility                   |
| <input type="radio"/> | B. Longer half-life                             |
| <input type="radio"/> | C. Decreased post-prandial acid production      |
| <input type="radio"/> | D. Irreversible blockade of $H^+/K^+$ ATPase    |
| <input type="radio"/> | E. More effective histamine receptor antagonism |

[Next question](#)

Proton pump inhibitors can reduce gastric acid secretion by up to 99%. Acid production resumes following the normal renewal of gastric parietal cells.

### Proton pump inhibitors

Proton pump inhibitors (PPI) are a group of drugs which profoundly reduce acid secretion in the stomach. They irreversibly blocking the hydrogen/potassium adenosine triphosphatase enzyme system (the  $H^+/K^+$  ATPase) of the gastric parietal cell

Examples include omeprazole and lansoprazole

In the Vaughan Williams classification of antiarrhythmics disopyramide is an example of a:

- ☐ A. Class Ia agent
- ☐ B. Class Ib agent
- ☐ C. Class Ic agent
- ☐ D. Class II agent
- ☐ E. Class IV agent

Next question

### Antiarrhythmics: Vaughan Williams classification

The Vaughan Williams classification of antiarrhythmics is still widely used although it should be noted that a number of common drugs are not included in the classification e.g. adenosine, atropine, digoxin and magnesium

Class	Example	Mechanism of action
Ia	Disopyramide	Block sodium channels
Ib	Lidocaine	Block sodium channels
Ic	Flecainide	Block sodium channels
II	Propranolol	Beta-adrenoceptor antagonists
III	Amiodarone	Block potassium channels
IV	Verapamil	Calcium channel blockers

A 34-year-old man with a history of migraine finds that paracetamol taken at the recommend dose often fails to relieve his acute attacks. He drinks 12 units of alcohol per week and smokes 15 cigarettes per day.

What factor is likely to contribute to this problem?

<input type="radio"/>	A. Bacterial overgrowth
<input type="radio"/>	B. Delayed gastric emptying
<input type="radio"/>	C. P450 enzyme induction
<input type="radio"/>	D. First pass metabolism
<input type="radio"/>	E. P450 enzyme inhibition

Patients with migraine experience delayed gastric emptying during acute attacks. For this reason analgesics are often combined prokinetic agents such as metoclopramide. Paracetamol metabolism would not be significantly affected by changes in P450 enzyme activity (e.g. through smoking or drinking)

### Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. NICE produced guidelines in 2012 on the management of headache, including migraines.

#### Acute treatment

- first-line: offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol
- for young people aged 12-17 years consider a nasal triptan in preference to an oral triptan
- if the above measures are not effective or not tolerated offer a non-oral preparation of metoclopramide\* or prochlorperazine and consider adding a non-oral NSAID or triptan

#### Prophylaxis

- prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients.
- NICE advise either topiramate or propranolol 'according to the person's preference, comorbidities and risk of adverse events'. Propranolol should be used in preference to topiramate in women of child bearing age as it may be teratogenic and it can reduce the effectiveness of hormonal contraceptives
- if these measures fail NICE recommend 'a course of up to 10 sessions of acupuncture over 5-8 weeks' or gabapentin
- NICE recommend: 'Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people'
- for women with predictable menstrual migraine treatment NICE recommend either frovatriptan (2.5 mg twice a day) or zolmitriptan (2.5 mg twice or three times a day) as a type of 'mini-prophylaxis'
- pizotifen is no longer recommend. Adverse effects such as weight gain & drowsiness are common

\*caution should be exercised with young patients as acute dystonic reactions may develop



A 55-year-old diabetic man presents to clinic concerned about erectile dysfunction. What is the mechanism of action of sildenafil?

<input type="radio"/>	A. Phosphodiesterase type V inhibitor
<input type="radio"/>	B. Nitric oxide synthetase inhibitor
<input type="radio"/>	C. Nitric oxide donor
<input type="radio"/>	D. Non-selective phosphodiesterase inhibitor
<input type="radio"/>	E. Phosphodiesterase type IV inhibitor

[Next question](#)

Sildenafil is a phosphodiesterase type V inhibitor

### Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

#### Contraindications

- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

#### Side-effects

- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects
- headache

Which of the following drugs is least likely to cause cholestasis?

<input type="radio"/>	A. Anabolic steroids
<input type="radio"/>	B. Erythromycin
<input type="radio"/>	C. Prochlorperazine
<input type="radio"/>	D. Halothane
<input type="radio"/>	E. Flucloxacillin

### Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyl dopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin\*, nitrofurantoin
- anabolic steroids, testosterone
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyl dopa
- amiodarone

\*risk may be reduced with erythromycin stearate

A 30-year-old woman who is 34 weeks pregnant presents with dysuria and urinary frequency. A urine dipstick is positive for nitrites and leucocytes. Of the options given, what is the most suitable antibiotic to use?

<input type="radio"/>	A. Ciprofloxacin
<input type="radio"/>	B. Cefalexin
<input type="radio"/>	C. Trimethoprim + folic acid 5mg
<input type="radio"/>	D. Doxycycline
<input type="radio"/>	E. Nitrofurantoin

[Next question](#)

Amoxicillin is also recommended in this situation. Nitrofurantoin should be avoided near term.

### Urinary tract infection in adults: management

Lower urinary tract infections in women (cystitis)

- local antibiotic guidelines should be followed if available
- Clinical Knowledge Summaries (CKS) recommend trimethoprim or nitrofurantoin for 3 days

Lower urinary tract infections in pregnancy

- asymptomatic bacteriuria is screened for on the booking visit. If found, it should be confirmed with a second MSU and treated if confirmed (please see CKS link for more details)
- for acute lower urinary tract infections consider amoxicillin or an oral cephalosporin for 7 days\*

For patients with sign of acute pyelonephritis hospital admission should be considered

- local antibiotic guidelines should be followed if available
- the BNF currently recommends a broad-spectrum cephalosporin or a quinolone for 10-14 days
- Clinical Knowledge Summaries recommend ciprofloxacin for 7 days or co-amoxiclav for 14 days

\*CKS also mention the use of trimethoprim and nitrofurantoin. Trimethoprim is a folate antagonist and concerns have been raised regarding the potential risk of neural tube defects. Manufacturers advise to avoid. Whilst short-term trimethoprim use is unlikely to cause folate deficiency it would seem reasonable to use an antibiotic such as amoxicillin first-line. Nitrofurantoin should be avoided at term because of the risk of neonatal haemolysis

Thrombocytopenia is associated with each of the following drugs except:

<input type="radio"/>	A. Abciximab
<input type="radio"/>	B. Quinine
<input type="radio"/>	C. Warfarin
<input type="radio"/>	D. Penicillin
<input type="radio"/>	E. Sodium valproate

Next question

### Drug-induced thrombocytopenia

Drug-induced thrombocytopenia (probable immune mediated)

- quinine
- abciximab
- NSAIDS
- diuretics: furosemide
- antibiotics: penicillins, sulphonamides, rifampicin
- anticonvulsants: carbamazepine, valproate
- heparin

Which one of the following medications is least associated with the development of methaemoglobinaemia?

<input type="radio"/>	A. Phenytoin
<input type="radio"/>	B. Sulphonamides
<input type="radio"/>	C. Dapsone
<input type="radio"/>	D. Sodium nitroprusside
<input type="radio"/>	E. Primaquine

Next question

### Methaemoglobinaemia

Methaemoglobinaemia describes haemoglobin which has been oxidised from  $\text{Fe}^{2+}$  to  $\text{Fe}^{3+}$ . This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as  $\text{Fe}^{3+}$  cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

#### Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

#### Acquired causes

- drugs: sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

#### Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal  $\text{pO}_2$  but decreased oxygen saturation

#### Management

- NADH - methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylene blue if acquired

A 43-year-old man presents with known acute intermittent porphyria is brought to the Emergency Department by the police due to an acute psychosis. What is the most suitable drug for sedation?

<input type="radio"/>	A. Chloral hydrate
<input type="radio"/>	B. Diazepam
<input type="radio"/>	C. Phenobarbitone
<input checked="" type="radio"/>	D. Chlorpromazine
<input type="radio"/>	E. Primidone

[Next question](#)

Chlorpromazine is considered safe to use in patients with acute intermittent porphyria. The other drugs are classified as unsafe

#### Acute intermittent porphyria: drugs

Acute intermittent porphyria (AIP) is an autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40 year olds. AIP is more common in females (5:1)

Drugs which may precipitate attack

- barbiturates
- halothane
- benzodiazepines
- alcohol
- oral contraceptive pill
- sulphonamides

Drugs considered safe to use

- paracetamol
- aspirin
- codeine
- morphine
- chlorpromazine
- beta-blockers
- penicillin
- metformin

A 54-year-old man is diagnosed with type 2 diabetes mellitus. A decision is made to start simvastatin 40mg. What is the ideal time to advise patients to take this medication?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. After breakfast            |
| <input type="radio"/> | B. Last thing in the evening  |
| <input type="radio"/> | C. After evening meal         |
| <input type="radio"/> | D. Just before evening meal   |
| <input type="radio"/> | E. First thing in the morning |

[Next question](#)

Taking simvastatin at night improves efficacy

## Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

### Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

### Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk  $\geq 20\%$
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM > 40-years-old were prescribed statins. Now patients > 40-years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk < 20%/10 years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering\*

	<b>Total cholesterol (mmol/l)</b>	<b>LDL cholesterol</b>
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

\*current NICE guidelines do not recommend a target cholesterol in primary prevention



A patient who is intolerant of aspirin is started on clopidogrel for the secondary prevention of ischaemic heart disease. Concurrent use of which one of the following drugs may make clopidogrel less effective?

<input type="radio"/>	A. Warfarin
<input type="radio"/>	B. Omeprazole
<input type="radio"/>	C. Codeine
<input type="radio"/>	D. Long-term tetracycline use (e.g. For acne rosacea)
<input type="radio"/>	E. Selective serotonin reuptake inhibitors

[Next question](#)

## Clopidogrel

Clopidogrel is an antiplatelet agent used in the management of cardiovascular disease. It was previously used when aspirin was not tolerated or contraindicated but there are now a number of conditions for which clopidogrel is used in addition to aspirin, for example in patients with an acute coronary syndrome. Following the 2010 NICE technology appraisal clopidogrel is also now first-line in patients following an ischaemic stroke and in patients with peripheral arterial disease.

### Mechanism

- inhibits ADP binding to its platelet receptor

### Interactions

- concurrent use of proton pump inhibitors (PPIs) may make clopidogrel less effective (MHRA July 2009)
- this advice was updated by the MHRA in April 2010, evidence seems inconsistent but omeprazole and esomeprazole still cause for concern. Other PPIs such as lansoprazole should be OK - please see the link for more details

A 14-year-old is seen in the Emergency Department. She was diagnosed with having migraines three years ago and requests advice about options for treating an acute attack. Which one of the following medications is it least suitable to recommend?

<input type="radio"/>	A. Aspirin
<input type="radio"/>	B. Paracetamol + prochlorperazine
<input type="radio"/>	C. Paracetamol + codeine
<input type="radio"/>	D. Ibuprofen
<input type="radio"/>	E. Paracetamol

[Next question](#)

Avoid aspirin in children < 16 years as risk of Reye's syndrome

Aspirin should be avoided in children due to the risk of Reye's syndrome. Codeine would also be a poor choice as it has limited benefit in migraine.

### Migraine: management

It should be noted that as a general rule 5-HT receptor agonists are used in the acute treatment of migraine whilst 5-HT receptor antagonists are used in prophylaxis. NICE produced guidelines in 2012 on the management of headache, including migraines.

#### Acute treatment

- first-line: offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol
- for young people aged 12-17 years consider a nasal triptan in preference to an oral triptan
- if the above measures are not effective or not tolerated offer a non-oral preparation of metoclopramide\* or prochlorperazine and consider adding a non-oral NSAID or triptan

#### Prophylaxis

- prophylaxis should be given if patients are experiencing 2 or more attacks per month. Modern treatment is effective in about 60% of patients.
- NICE advise either topiramate or propranolol 'according to the person's preference, comorbidities and risk of adverse events'. Propranolol should be used in preference to topiramate in women of child bearing age as it may be teratogenic and it can reduce the effectiveness of hormonal contraceptives
- if these measures fail NICE recommend 'a course of up to 10 sessions of acupuncture over 5-8 weeks' or gabapentin

- NICE recommend: 'Advise people with migraine that riboflavin (400 mg once a day) may be effective in reducing migraine frequency and intensity for some people'
- for women with predictable menstrual migraine treatment NICE recommend either frovatriptan (2.5 mg twice a day) or zolmitriptan (2.5 mg twice or three times a day) as a type of 'mini-prophylaxis'
- pizotifen is no longer recommend. Adverse effects such as weight gain & drowsiness are common

\*caution should be exercised with young patients as acute dystonic reactions may develop

A 54-year-old man is investigated for recurrent episodes of abdominal pain associated with weakness of his arms and legs. Which one of the following urine tests would best indicate lead toxicity?

<input type="radio"/>	A. Haemoglobinuria
<input type="radio"/>	B. Coproporphyrin
<input type="radio"/>	C. Porphobilinogen
<input type="radio"/>	D. Uroporphyrin
<input type="radio"/>	E. Ham's test

### Lead poisoning

Along with acute intermittent porphyria, lead poisoning should be considered in questions giving a combination of abdominal pain and neurological signs

#### Features

- abdominal pain
- peripheral neuropathy (mainly motor)
- fatigue
- constipation
- blue lines on gum margin (only 20% of adult patients, very rare in children)

#### Investigations

- the blood lead level is usually used for diagnosis. Levels greater than 10 mcg/dl are considered significant
- full blood count: microcytic anaemia. Blood film shows red cell abnormalities including basophilic stippling and clover-leaf morphology
- raised serum and urine levels of delta aminolaevulinic acid may be seen making it sometimes difficult to differentiate from acute intermittent porphyria
- urinary coproporphyrin is also increased (urinary porphobilinogen and uroporphyrin levels are normal to slightly increased)

Management - various chelating agents are currently used:

- dimercaptosuccinic acid (DMSA)
- D-penicillamine
- EDTA
- dimercaprol

Which one of the following side-effects is not recognised in patients taking sodium valproate?

<input type="radio"/>	A. Alopecia
<input type="radio"/>	B. Weight gain
<input type="radio"/>	C. Hepatitis
<input type="radio"/>	D. Induction P450 system
<input type="radio"/>	E. Teratogenicity

Next question

Sodium valproate causes inhibition of the P450 system

### Sodium valproate

Sodium valproate is used in the management of epilepsy and is first line therapy for generalised seizures. It works by increasing GABA activity.

#### Adverse effects

- gastrointestinal: nausea
- increased appetite and weight gain
- alopecia: regrowth may be curly
- ataxia
- tremor
- hepatitis
- pancreatitis
- thrombocytopaenia
- teratogenic

Each of the following drugs are known to inhibit cytochrome P450, except:

<input type="radio"/>	A. Ketoconazole
<input type="radio"/>	B. Ciprofloxacin
<input type="radio"/>	C. Erythromycin
<input type="radio"/>	D. Clopidogrel
<input type="radio"/>	E. Amiodarone

Next question

### P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

A 45-year-old female with a history of bipolar disorder presents with an acute confusional state. Which one of the following drugs is most likely to precipitate lithium toxicity?

<input type="radio"/>	A. Sodium valproate
<input type="radio"/>	B. Atenolol
<input type="radio"/>	C. Aminophylline
<input type="radio"/>	D. Sodium bicarbonate
<input type="radio"/>	E. Bendroflumethiazide

[Next question](#)

Both sodium bicarbonate and aminophylline may reduce plasma concentrations of lithium. Sodium valproate is not listed in the BNF as interacting with lithium

### Lithium toxicity

Lithium is mood stabilising drug used most commonly prophylactically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys. Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

#### Features of toxicity

- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

#### Management

- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

A 49-year-old homeless man is admitted to the ITU after drinking a large quantity of methanol. Treatment with fomepizole is started. What is the mechanism of action of fomepizole?

- |                                  |   |
|----------------------------------|---|
| <input type="radio"/>            | A. Chelates methanol                                |
| <input checked="" type="radio"/> | B. Competitive inhibition of alcohol dehydrogenase  |
| <input type="radio"/>            | C. Converts methanol to ethanol                     |
| <input type="radio"/>            | D. Competitive inhibition of aldehyde dehydrogenase |
| <input type="radio"/>            | E. Formaldehyde dehydrogenase inhibitor             |

[Next question](#)

Fomepizole - used in ethylene glycol and methanol poisoning - competitive inhibitor of alcohol dehydrogenase

### Methanol poisoning

Methanol poisoning causes both the effects associated with alcohol (intoxication, nausea etc) and also specific visual problems, including blindness. These effects are thought to be secondary to the accumulation of formic acid. The actual pathophysiology of methanol-associated visual loss is not fully understood but it is thought to be caused by a form of optic neuropathy

#### Management

- fomepizole or ethanol
- haemodialysis



A 26-year-old woman with a history of schizophrenia is reviewed in the Emergency Department. Her carer reports that she has been 'staring' for the past few hours but has now developed abnormal head movements and has gone 'cross-eyed'. On examination the patient's neck is extended and positioned to the right. Her eyes are deviated upwards and are slightly converged. Given the likely diagnosis, what is the most appropriate treatment?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Procyclidine |
| <input type="radio"/> | B. Dopamine     |
| <input type="radio"/> | C. Selegiline   |
| <input type="radio"/> | D. Haloperidol  |
| <input type="radio"/> | E. Diazepam     |

[Next question](#)

Benztropine and diphenhydramine are alternative options.

### Oculogyric crisis

An oculogyric crisis is a dystonic reaction to certain drugs or medical conditions

#### Features

- restlessness, agitation
- involuntary upward deviation of the eyes

#### Causes

- phenothiazines
- haloperidol
- metoclopramide
- postencephalitic Parkinson's disease

#### Management

- procyclidine

Which one of the following statements regarding the management of pregnant women with severe pre-eclampsia and eclampsia is incorrect?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Intravenous fluids should be given to prevent renal failure           |
| <input type="radio"/> | B. Magnesium sulphate treatment should continue for 24 hours post-partum |
| <input type="radio"/> | C. Problems are only seen after 20 weeks gestation                       |
| <input type="radio"/> | D. Reflexes should be monitored during magnesium sulphate infusion       |
| <input type="radio"/> | E. Magnesium sulphate is given to both prevent and treat seizures        |

[Next question](#)

Severe pre-eclampsia - restrict fluids

Pulmonary and cerebral oedema are important causes of morbidity and mortality in severe pre-eclampsia

## Eclampsia

Eclampsia may be defined as the development of seizures in association pre-eclampsia. To recap, pre-eclampsia is defined as:

- condition seen after 20 weeks gestation
- pregnancy-induced hypertension
- proteinuria

Magnesium sulphate is used to both prevent seizures in patients with severe pre-eclampsia and treat seizures once they develop. Guidelines on its use suggest the following:

- should be given once a decision to deliver has been made
- in eclampsia an IV bolus of 4g over 5-10 minutes should be given followed by an infusion of 1g / hour
- urine output, reflexes, respiratory rate and oxygen saturations should be monitored during treatment
- treatment should continue for 24 hours after last seizure or delivery (around 40% of seizures occur post-partum)

Other important aspects of treating severe pre-eclampsia/eclampsia include fluid restriction to avoid the potentially serious consequences of fluid overload

A 33-year-old woman is prescribed varenicline to help her quit smoking. What is the mechanism of action of varenicline?

<input type="radio"/>	A. Norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
<input type="radio"/>	B. Dopamine agonist
<input type="radio"/>	C. Dopamine antagonist
<input type="radio"/>	D. Selective serotonin reuptake inhibitor
<input type="radio"/>	E. Nicotinic receptor partial agonist

[Next question](#)

## Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

### Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

### Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop
- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)

- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

## Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication

A 70-year-old woman is prescribed bumetanide for congestive cardiac failure. Where is the site of action of bumetanide?

<input type="radio"/>	A. Descending loop of Henle
<input type="radio"/>	B. Macula densa
<input type="radio"/>	C. Ascending loop of Henle
<input type="radio"/>	D. Distal collecting duct
<input type="radio"/>	E. Proximal collecting duct

[Next question](#)

Bumetanide, like furosemide, is a loop diuretic.

### Loop diuretics

Furosemide and bumetanide are loop diuretics that act by inhibiting the Na-K-Cl cotransporter in the thick ascending limb of the loop of Henle, reducing the absorption of NaCl.

#### Indications

- heart failure: both acute (usually intravenously) and chronic (usually orally)
- resistant hypertension, particularly in patients with renal impairment

#### Adverse effects

- hypotension
- hyponatraemia
- hypokalaemia
- hypochloraemic alkalosis
- ototoxicity
- hypocalcaemia
- renal impairment (from dehydration + direct toxic effect)
- hyperglycaemia (less common than with thiazides)
- gout

What is the mechanism of action of tacrolimus?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Mercaptopurine antagonist                        |
| <input type="radio"/> | B. Interferes with purine synthesis                 |
| <input type="radio"/> | C. Inhibits inosine monophosphate dehydrogenase     |
| <input type="radio"/> | D. Monoclonal antibody against IL-2 receptor        |
| <input type="radio"/> | E. Decreases IL-2 release by inhibiting calcineurin |

Next question

### Tacrolimus

Tacrolimus is a macrolide used as an immunosuppressant to prevent transplant rejection. It has a very similar action to ciclosporin:

Action of ciclosporin

- decreases clonal proliferation of T cells by reducing IL-2 release
- binds to cyclophilin forming a complex which inhibits calcineurin, a phosphatase that activates various transcription factors in T cells

The action of tacrolimus differs in that it binds to a protein called FKBP rather than cyclophilin

Tacrolimus is more potent than ciclosporin and hence the incidence of organ rejection is less. However, nephrotoxicity and impaired glucose tolerance is more common

A 71-year-old man is prescribed digoxin for new onset atrial fibrillation. His doctor explains that the full effect will not be seen for one week. Which one of the following is responsible for this delayed effect?

<input type="radio"/>	A. Clearance
<input type="radio"/>	B. Volume of distribution
<input type="radio"/>	C. Absorption
<input type="radio"/>	D. First pass metabolism
<input type="radio"/>	E. Half-life

[Next question](#)

The half-life of digoxin is around 36-48 hours. This results in a delay before steady plasma levels are seen

### Digoxin and digoxin toxicity

Digoxin is a cardiac glycoside now mainly used for rate control in the management of atrial fibrillation. As it has positive inotropic properties it is sometimes used for improving symptoms (but not mortality) in patients with heart failure.

#### Mechanism of action

- decreases conduction through the atrioventricular node which slows the ventricular rate in atrial fibrillation and flutter
- increases the force of cardiac muscle contraction due to inhibition of the  $\text{Na}^+/\text{K}^+\text{ATPase}$  pump

### Digoxin toxicity

Plasma concentration alone does not determine whether a patient has developed digoxin toxicity. The BNF advises that the likelihood of toxicity increases progressively from 1.5 to 3 mcg/l.

#### Features

- generally unwell, lethargy, nausea & vomiting, anorexia, confusion, yellow-green vision
- arrhythmias (e.g. AV block, bradycardia)

#### Precipitating factors

- classically: hypokalaemia\*
- increasing age
- renal failure
- myocardial ischaemia
- hypomagnesaemia, hypercalcaemia, hypernatraemia, acidosis

- hypoalbuminaemia
- hypothermia
- hypothyroidism
- drugs: amiodarone, quinidine, verapamil, diltiazem, spironolactone (compete for secretion in distal convoluted tubule therefore reduce excretion). Also drugs which cause hypokalaemia e.g. thiazides and loop diuretics

## Management

- Digibind
- correct arrhythmias
- monitor potassium

\*hyperkalaemia may also worsen digoxin toxicity, although this is very small print



A 62-year-old female is reviewed in the nurse-led heart failure clinic. Despite current treatment with furosemide, bisoprolol, enalapril and spironolactone she remains breathless on minimal exertion. On examination the chest is clear to auscultation and there is minimal ankle oedema

Recent results are as follows:

ECG	Sinus rhythm, rate 84 bpm
Chest x-ray	Cardiomegaly, clear lung fields
Echo	Ejection fraction 35%

A combination of isosorbide dinitrate with hydralazine has been tried recently but had to be stopped due to side-effects. What additional medication would best help her symptoms?

- ☐ A. Bosentan
- ☐ B. Isosorbide mononitrate
- ☐ C. Diltiazem
- ☐ D. Ivabradine
- ☐ E. Digoxin

Next question

Digoxin may be useful in this situation whether the patient is in atrial fibrillation or not. Whilst it has not been shown to be of prognostic benefit it may help reduce symptoms. In the United States a large proportion of patients with heart failure take digoxin for this reason. Another option to consider in such a patient would be a biventricular pacemaker (cardiac resynchronization therapy)

### Heart failure: drug management

A number of drugs have been shown to improve mortality in patients with chronic heart failure:

- ACE inhibitors (SAVE, SOLVD, CONSENSUS)
- spironolactone (RALES)
- beta-blockers (CIBIS)
- hydralazine with nitrates (VHEFT-1)

No long-term reduction in mortality has been demonstrated for loop diuretics such as furosemide.

NICE issued updated guidelines on management in 2010, key points include:

- first-line treatment for all patients is both an ACE-inhibitor and a beta-blocker
- second-line treatment is now either an aldosterone antagonist, angiotensin II receptor blocker or a hydralazine in combination with a nitrate

- if symptoms persist cardiac resynchronisation therapy or digoxin\* should be considered
- diuretics should be given for fluid overload
- offer annual influenza vaccine
- offer one-off\*\* pneumococcal vaccine

\*digoxin has also not been proven to reduce mortality in patients with heart failure. It may however improve symptoms due to its inotropic properties. Digoxin is strongly indicated if there is coexistent atrial fibrillation

\*\*adults usually require just one dose but those with asplenia, splenic dysfunction or chronic kidney disease need a booster every 5 years

**Question 213 of 265**

Next

A 36-year-old man with difficult to control epilepsy is reviewed in clinic. He is currently taking phenytoin but presents due to fatigue. A full blood count is performed:

Hb	10.1 g/dl
MCV	121 fl
Plt	$234 \times 10^9/l$
WCC	$4.6 \times 10^9/l$

What is the most likely cause for his tiredness?

- ☐ A. Iron deficiency
- ☐ B. Vitamin B12 deficiency
- ☐ C. Liver dysfunction secondary to phenytoin
- ☐ D. Haemolytic anaemia secondary to phenytoin
- ☐ E. Folate deficiency

Next question

**Phenytoin**

Phenytoin is used to in the management of seizures.

Mechanism of action

- sodium channel blocker, decreasing the sodium influx into neurons which in turn decreases excitability

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute

- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic

- common: gingival hyperplasia (secondary to increased expression of platelet derived growth factor, PDGF), hirsutism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)

- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

#### Idiosyncratic

- fever
- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture\*
- aplastic anaemia
- drug-induced lupus

#### Teratogenic

- associated with cleft palate and congenital heart disease

\*although not listed in the BNF

A 44-year-old woman with oestrogen receptor positive breast cancer comes for review, three months after starting tamoxifen. Which one of the following adverse effects is most likely to occur in this patient?

<input type="radio"/>	A. Myalgia
<input type="radio"/>	B. Cataracts
<input type="radio"/>	C. Alopecia
<input checked="" type="radio"/>	D. Hot flushes
<input type="radio"/>	E. Cervical cancer

[Next question](#)

Alopecia and cataracts are listed in the BNF as possible side-effects. They are however not as prevalent as hot flushes, which are very common in pre-menopausal women

### Tamoxifen

Tamoxifen is a selective estrogen receptor modulator (SERM) which acts as an oestrogen receptor antagonist and partial agonist. It is used in the management of oestrogen receptor positive breast cancer

#### Adverse effects

- menstrual disturbance: vaginal bleeding, amenorrhoea
- hot flushes
- venous thromboembolism
- endometrial cancer

Tamoxifen is typically used for 5 years following removal of the tumour.

Raloxifene is a pure oestrogen receptor antagonist, and carries a lower risk of endometrial cancer

Where is the site of action of bendroflumethiazide?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Proximal convoluted tubules                    |
| <input type="radio"/> | B. Ascending loop of Henle                        |
| <input type="radio"/> | C. Descending loop of Henle                       |
| <input type="radio"/> | D. Proximal part of the distal convoluted tubules |
| <input type="radio"/> | E. Distal part of the distal convoluted tubules   |

Next question

Bendroflumethiazide - site of action = proximal part of the distal convoluted tubules

### Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide was in the management of hypertension but recent NICE guidelines now recommend other thiazide-like diuretics such as indapamide and chlortalidone.

#### Common adverse effects

- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

#### Rare adverse effects

- thrombocytopenia
- agranulocytosis
- photosensitivity rash
- pancreatitis

(An eagle eyed user noticed that this entry is very similar to the Wikipedia one. I can assure you that the material has been cut-and-pasted from passmedicine to Wikipedia, and not vice-versa! Note the English spellings of hyponatraemia etc. Check the Wikipedia 'history' page for more details.)

What is the most appropriate time to take blood samples for therapeutic monitoring of phenytoin levels?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. At any time                  |
| <input type="radio"/> | B. 12 hours after last dose     |
| <input type="radio"/> | C. 6 hours after last dose      |
| <input type="radio"/> | D. 4 hours after last dose      |
| <input type="radio"/> | E. Immediately before next dose |

Next question

### Therapeutic drug monitoring

#### Lithium

- range = 0.4 - 1.0 mmol/l
- take 12 hrs post-dose

#### Ciclosporin

- trough levels immediately before dose

#### Digoxin

- at least 6 hrs post-dose

#### Phenytoin

- trough levels immediately before dose

A 45-year-old man with a known history of seafood allergy is admitted to the Emergency Department. He developed an itchy skin rash whilst having dinner at a restaurant. On examination he has widespread urticaria but no facial or neck swelling. His respiratory rate is 30 per minute with oxygen sats of 99% on room air. The blood pressure is 168/90 mmHg and the pulse 104 bpm. Intravenous hydrocortisone and chlorpheniramine are given. What is the most appropriate next step in management?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Inhaled adrenaline       |
| <input type="radio"/> | B. Observe                  |
| <input type="radio"/> | C. Subcutaneous adrenaline  |
| <input type="radio"/> | D. Intravenous adrenaline   |
| <input type="radio"/> | E. Intramuscular adrenaline |

Giving adrenaline is not without its risks, but very few severe adverse effects are seen with intramuscular adrenaline

We've had much feedback regarding this question, with many doctors stating they would give IM adrenaline in a real life situation. It is the opinion of the authors that the question is testing candidates knowledge of the ALS protocol and hence we would recommend giving the above answer in an exam situation. What do you think? Let us know

It could of course be argued that a raised respiratory rate and tachycardia are early signs of shock in a young person, but these may be secondary to anxiety

What do you think? - let us know.

## Adrenaline

Adrenaline is a sympathomimetic amine with both alpha and beta adrenergic stimulating properties

### Indications

- anaphylaxis
- cardiac arrest

### Recommend Adult Life Support (ALS) adrenaline doses

- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

### Management of accidental injection

- local infiltration of phentolamine



Which one of the following is least associated with an increased risk of hepatotoxicity following a paracetamol overdose?

<input type="radio"/>	A. History of alcohol dependence
<input type="radio"/>	B. Carbamazepine use
<input type="radio"/>	C. Anorexia nervosa
<input type="radio"/>	D. Chronic renal failure
<input type="radio"/>	E. HIV

[Next question](#)

Paracetamol overdose - high risk if chronic alcohol, HIV, anorexia or P450 inducers

### Paracetamol overdose: risk factors

The following groups of patients are at an increased risk of developing hepatotoxicity following a paracetamol overdose:

- patients taking liver enzyme-inducing drugs (rifampicin, phenytoin, carbamazepine, chronic alcohol excess, St John's Wort)
- malnourished patients (e.g. anorexia or bulimia, cystic fibrosis, hepatitis C, alcoholism, HIV)
- patients who have not eaten for a few days

Which one of the following may reduce the effects of adenosine?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Dipyridamole  |
| <input type="radio"/> | B. Diltiazem     |
| <input type="radio"/> | C. Clopidogrel   |
| <input type="radio"/> | D. Amiodarone    |
| <input type="radio"/> | E. Aminophylline |

Next question

#### Adenosine

- dipyridamole enhances effect
- aminophylline reduces effect

#### Adenosine

The effects of adenosine are enhanced by dipyridamole (anti-platelet agent) and blocked by theophyllines. It should be avoided in asthmatics due to possible bronchospasm.

#### Mechanism of action

- causes transient heart block in the AV node
- agonist of the A1 receptor which inhibits adenylyl cyclase thus reducing cAMP and causing hyperpolarization by increasing outward potassium flux
- adenosine has a very short half-life of about 8-10 seconds

#### Adverse effects

- chest pain
- bronchospasm
- can enhance conduction down accessory pathways, resulting in increased ventricular rate (e.g. WPW syndrome)

A 24-year-old woman presents following a sudden, acute onset of pain at the back of the ankle whilst jogging, during which she heard a cracking sound. Which one of the following medications may have contributed to this injury?

<input type="radio"/>	A. Metronidazole
<input type="radio"/>	B. Nitrofurantoin
<input type="radio"/>	C. Fluconazole
<input checked="" type="radio"/>	D. Ciprofloxacin
<input type="radio"/>	E. Terbinafine

[Next question](#)

Ciprofloxacin - tendinopathy

This patient has classical signs of Achilles tendon rupture. Tendon damage is a well documented complication of quinolone therapy. It appears to be an idiosyncratic reaction, with the actual median duration of treatment being 8 days before problems occur

### Quinolones

Quinolones are a group of antibiotics which work by inhibiting DNA synthesis and are bactericidal in nature. Examples include:

- ciprofloxacin
- levofloxacin

### Adverse effects

- lower seizure threshold in patients with epilepsy
- tendon damage (including rupture) - the risk is increased in patients also taking steroids

A 45-year-old man develops toxic epidermal necrolysis following a change in his epilepsy medication. He is systemically unwell and is admitted to ITU for supportive care. What is the most appropriate treatment?

<input type="radio"/>	A. Intravenous immunoglobulin
<input type="radio"/>	B. Cyclophosphamide
<input type="radio"/>	C. Supportive care only
<input type="radio"/>	D. Pulsed methylprednisolone
<input type="radio"/>	E. Plasmapheresis

[Next question](#)

### Toxic epidermal necrolysis

Toxic epidermal necrolysis (TEN) is a potentially life-threatening skin disorder that is most commonly seen secondary to a drug reaction. In this condition the skin develops a scalded appearance over an extensive area. Some authors consider TEN to be the severe end of a spectrum of skin disorders which includes erythema multiforme and Stevens-Johnson syndrome

#### Features

- systemically unwell e.g. pyrexia, tachycardic
- positive Nikolsky's sign: the epidermis separates with mild lateral pressure

#### Drugs known to induce TEN

- phenytoin
- sulphonamides
- allopurinol
- penicillins
- carbamazepine
- NSAIDs

#### Management

- stop precipitating factor
- supportive care, often in intensive care unit
- intravenous immunoglobulin has been shown to be effective and is now commonly used first-line
- other treatment options include: immunosuppressive agents (ciclosporin and cyclophosphamide), plasmapheresis

A patient is given ondansetron for chemotherapy related nausea. What is the most likely side-effect?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Constipation       |
| <input type="radio"/> | B. Dry mouth          |
| <input type="radio"/> | C. Insomnia           |
| <input type="radio"/> | D. Visual disturbance |
| <input type="radio"/> | E. Pruritus           |

Next question

Whilst all the above may occur constipation is most common

### 5-HT3 antagonists

5-HT3 antagonists are antiemetics used mainly in the management of chemotherapy related nausea.

Examples

- ondansetron
- granisetron

A confused 45-year-old man is admitted to the Emergency Department. He tells staff he has drunk two bottles of antifreeze. On examination his pulse is 120 bpm and blood pressure is 140/90 mmHg. Arterial blood gases show an uncompensated metabolic acidosis. He is transferred to the high dependency unit and ethanol is given via a nasogastric tube. What is the mechanism of action of ethanol in this patient?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Binds to glycolic acid                                  |
| <input type="radio"/> | B. Inhibits aldehyde dehydrogenase                         |
| <input type="radio"/> | C. Inhibits alcohol dehydrogenase                          |
| <input type="radio"/> | D. Competes with ethylene glycol for alcohol dehydrogenase |
| <input type="radio"/> | E. Binds to glycoaldehyde                                  |

[Next question](#)

### Ethylene glycol toxicity

Ethylene glycol is a type of alcohol used as a coolant or antifreeze

Features of toxicity are divided into 3 stages:

- Stage 1: symptoms similar to alcohol intoxication: confusion, slurred speech, dizziness
- Stage 2: metabolic acidosis with high anion gap and high osmolar gap. Also tachycardia, hypertension
- Stage 3: acute renal failure

Management has changed in recent times

- ethanol has been used for many years
- works by competing with ethylene glycol for the enzyme alcohol dehydrogenase
- this limits the formation of toxic metabolites (e.g. glycoaldehyde and glycolic acid) which are responsible for the haemodynamic/metabolic features of poisoning
- **fomepizole**, an inhibitor of alcohol dehydrogenase, is now used first-line in preference to ethanol
- haemodialysis also has a role in refractory cases

Which one of the following drugs does not characteristically undergo extensive first-pass metabolism?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Propranolol         |
| <input type="radio"/> | B. Glyceryl trinitrate |
| <input type="radio"/> | C. Diazepam            |
| <input type="radio"/> | D. Aspirin             |
| <input type="radio"/> | E. Verapamil           |

Next question

### Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

### First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are needed orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil
- isoprenaline
- testosterone
- hydrocortisone

Questions concerning zero-order kinetics and acetylator status are also common in the exam

## **Zero-order kinetics**

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

## **Acetylator status**

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine



Which of the following drugs is most likely to cause impaired glucose tolerance?

<input type="radio"/>	A. Bromocriptine
<input type="radio"/>	B. Interferon-alpha
<input type="radio"/>	C. Strontium
<input type="radio"/>	D. Imipramine
<input type="radio"/>	E. Montelukast

Next question

### Drug-induced impaired glucose tolerance

Drugs which are known to cause impaired glucose tolerance include:

- thiazides, furosemide (less common)
- steroids
- tacrolimus, ciclosporin
- interferon-alpha
- nicotinic acid
- atypical antipsychotics e.g. olanzapine

Beta-blockers cause a slight impairment of glucose tolerance. They should also be used with caution in diabetics as they can interfere with the metabolic and autonomic responses to hypoglycaemia

A 71-year-old woman who takes warfarin for atrial fibrillation presents with lethargy. A blood test is arranged:

Hb	14.7 g/dl
Plt	$198 \times 10^9/l$
WBC	$5.3 \times 10^9/l$
INR	6.1

What is the most appropriate management?

- ☐ A. Stop warfarin + restart when INR < 3.0
- ☐ B. Intravenous vitamin K 0.5mg + stop warfarin + restart when INR < 5.0
- ☐ C. Withhold 2 doses of warfarin and reduce subsequent maintenance dose
- ☐ D. Stop warfarin + restart when INR < 5.0 + give low-molecular weight heparin until warfarin restarted
- ☐ E. Oral vitamin K 5mg + stop warfarin + restart when INR < 3.0

If the INR is between 5.0-8.0 and there is no bleeding the BNF advises that 1-2 doses of warfarin should be withheld and the subsequent maintenance doses reduced.

### Warfarin overdose

The following is based on the BNF guidelines, which in turn take into account the British Committee for Standards in Haematology (BCSH) guidelines. A 2005 update of the BCSH guidelines emphasised the preference of prothrombin complex concentrate over FFP in major bleeding.

<b>Major bleeding</b>	Stop warfarin Give intravenous vitamin K 5mg Prothrombin complex concentrate - if not available then FFP*
<b>INR &gt; 8.0</b> <b>Minor bleeding</b>	Stop warfarin Give intravenous vitamin K 1-3mg Repeat dose of vitamin K if INR still too high after 24 hours Restart warfarin when INR < 5.0
<b>INR &gt; 8.0</b> <b>No bleeding</b>	Stop warfarin Give oral vitamin K 1-5mg Repeat dose of vitamin K if INR still too high after 24 hours Restart when INR < 5.0
<b>INR 5.0-8.0</b> <b>Minor bleeding</b>	Stop warfarin Give intravenous vitamin K 1-3mg Restart when INR < 5.0

<b>INR 5.0-8.0</b> <b>No bleeding</b>	Withhold 1 or 2 doses of warfarin Reduce subsequent maintenance dose
--	---

\*as FFP can take time to defrost prothrombin complex concentrate should be considered in cases of intracranial haemorrhage

Each one of the following is a feature of mercury poisoning, except:

<input type="radio"/>	A. Paraesthesia
<input type="radio"/>	B. Epistaxis
<input type="radio"/>	C. Renal tubular acidosis
<input type="radio"/>	D. Visual field defects
<input type="radio"/>	E. Hearing loss

Next question

## Mercury poisoning

### Features

- paraesthesia
- visual field defects
- hearing loss
- irritability
- renal tubular acidosis

A 72-year-old man with metastatic small cell lung cancer is admitted to the local hospice for symptom control. His main problem at the moment is intractable hiccups. What is the most appropriate management?

- |                       |                      |
|-----------------------|----------------------|
| <input type="radio"/> | A. Chlorpromazine    |
| <input type="radio"/> | B. Codeine phosphate |
| <input type="radio"/> | C. Diazepam          |
| <input type="radio"/> | D. Methadone         |
| <input type="radio"/> | E. Phenytoin         |

[Next question](#)

Hiccups in palliative care - chlorpromazine or haloperidol

Haloperidol may also be used

### Palliative care prescribing: hiccups

Management of hiccups

- chlorpromazine is licensed for the treatment of intractable hiccups
- haloperidol, gabapentin and baclofen are also used

A 29-year-old woman is admitted to the Emergency Department with carbon monoxide poisoning. High-flow oxygen is applied on arrival. Which one of the following is not an indication for hyperbaric oxygen therapy?

<input type="radio"/>	A. A carboxyhaemoglobin concentration of 16%
<input type="radio"/>	B. Arrhythmia
<input type="radio"/>	C. Extrapyrimalidal features
<input type="radio"/>	D. Loss of consciousness when initially found by paramedics
<input type="radio"/>	E. Pregnancy

[Next question](#)

Heavy smokers may have a carboxyhaemoglobin concentration of 10-15%

### Carbon monoxide poisoning

Carbon monoxide has high affinity for haemoglobin and myoglobin resulting in a left-shift of the oxygen dissociation curve and tissue hypoxia. There are approximately 50 per year deaths from accidental carbon monoxide poisoning in the UK

Questions may hint at badly maintained housing e.g. student houses

Features of carbon monoxide toxicity

- headache: 90% of cases
- nausea and vomiting: 50%
- vertigo: 50%
- confusion: 30%
- subjective weakness: 20%
- severe toxicity: 'pink' skin and mucosae, hyperpyrexia, arrhythmias, extrapyramidal features, coma, death

Typical carboxyhaemoglobin levels

- < 3% non-smokers
- < 10% smokers
- 10 - 30% symptomatic: headache, vomiting
- > 30% severe toxicity

Management

- 100% oxygen
- hyperbaric oxygen

### Indications for hyperbaric oxygen\*

- loss of consciousness at any point
- neurological signs other than headache
- myocardial ischaemia or arrhythmia
- pregnancy

\*as stated in the 2008 Department of Health publication 'Recognising Carbon Monoxide Poisoning'

Which one of the following is not a recognised adverse effect of phenytoin use?

<input type="radio"/>	A. Slurred speech
<input type="radio"/>	B. Nystagmus
<input type="radio"/>	C. Gynaecomastia
<input type="radio"/>	D. Diplopia
<input type="radio"/>	E. Ataxia

Next question

## Phenytoin

Phenytoin is used to in the management of seizures.

Mechanism of action

- sodium channel blocker, decreasing the sodium influx into neurons which in turn decreases excitability

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute

- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic

- common: gingival hyperplasia (secondary to increased expression of platelet derived growth factor, PDGF), hirsutism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

Idiosyncratic

- fever



- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture\*
- aplastic anaemia
- drug-induced lupus

#### Teratogenic

- associated with cleft palate and congenital heart disease

\*although not listed in the BNF

A 75-year-old woman with a history of hypothyroidism is admitted to the Emergency Department following an episode of chest pain. She is diagnosed as having an acute coronary syndrome and iron-deficiency anaemia. A percutaneous coronary intervention is performed and a coronary artery stent is inserted. Endoscopies of the upper and lower gastrointestinal tract are performed and reported as normal. She is discharged on the following drugs in addition to her regular levothyroxine: aspirin, clopidogrel, ramipril, lansoprazole, simvastatin and ferrous sulphate. Six weeks later she complains of feeling tired all the time. Her GP arranges some routine blood tests:

Hb	11.9 g/dl
Platelets	155 * 10 <sup>9</sup> /l
WBC	5.2 * 10 <sup>9</sup> /l

Free T4	8.1 pmol/l
TSH	8.2 mu/l

Prior to her recent admission the TSH has been within range for the past two years. Which one of the following new drugs most likely explains the raised TSH?

- ☐ A. Simvastatin
- ☐ B. Clopidogrel
- ☐ C. Ferrous sulphate
- ☐ D. Ramipril
- ☐ E. Lansoprazole

[Next question](#)

Iron reduces the absorption of thyroxine

### Hypothyroidism: management

#### Key points

- initial starting dose of levothyroxine should be lower in elderly patients and those with ischaemic heart disease (e.g. 25-50 mcg/day)
- following a change in thyroxine dose thyroid function tests should be checked after 6-8 weeks
- the therapeutic goal is 'normalisation' of the thyroid stimulating hormone (TSH) level. As the majority unaffected people have a TSH value 0.5-2.5 mU/l it is now thought preferable to aim for a TSH in this range
- there is no evidence to support combination therapy with levothyroxine and liothyronine

### Side-effects of thyroxine therapy

- hyperthyroidism: due to over treatment
- reduced bone mineral density
- worsening of angina
- atrial fibrillation

### Interactions

- iron: absorption of levothyroxine reduced, give at least 2 hours apart

A 65-year-old female with metastatic breast cancer is reviewed in clinic. Her husband reports that she is increasingly confused and occasionally appears to talk to relatives that are not in the room. Following investigations for reversible causes, what is the most appropriate management?

<input type="radio"/>	A. Subcutaneous midazolam
<input type="radio"/>	B. Oral lithium
<input type="radio"/>	C. Oral haloperidol
<input type="radio"/>	D. Oral diazepam
<input type="radio"/>	E. Oral quetiapine

[Next question](#)

Oral haloperidol is the most appropriate treatment here. If the patient was in the terminal phase and agitated then subcutaneous midazolam would be indicated

#### **Palliative care prescribing: agitation and confusion**

Underlying causes of confusion need to be looked for and treated as appropriate, for example hypercalcaemia, infection, urinary retention and medication. If specific treatments fail then the following may be tried:

- first choice: haloperidol
- other options: chlorpromazine, levomepromazine

In the terminal phase of the illness (for example a patient on the Care of the Dying pathway) then agitation or restlessness is best treated with midazolam

A 56 year old man is treated with doxorubicin for transition cell carcinoma of the bladder. Which one of the following adverse effects is most characteristically associated with this drug?

- ☐ A. Ototoxicity
- ☐ B. Pulmonary fibrosis
- ☐ C. Peripheral neuropathy
- ☐ D. Cardiomyopathy
- ☐ E. Haemorrhagic cystitis

[Next question](#)

### Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

Which of the following anti-retroviral drugs is a known inducer of cytochrome P450?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Nevirapine |
| <input type="radio"/> | B. Ritonavir  |
| <input type="radio"/> | C. Saquinavir |
| <input type="radio"/> | D. Nelfinavir |
| <input type="radio"/> | E. Zidovudine |

Next question

HIV: anti-retrovirals - P450 interaction

- nevirapine (a NNRTI): induces P450
- protease inhibitors: inhibits P450

Like other protease inhibitors, ritonavir is a potent inhibitor of the P450 system

### HIV: anti-retrovirals

Highly active anti-retroviral therapy (HAART) involves a combination of at least three drugs, typically two nucleoside reverse transcriptase inhibitors (NRTI) and either a protease inhibitor (PI) or a non-nucleoside reverse transcriptase inhibitor (NNRTI). This combination both decreases viral replication but also reduces the risk of viral resistance emerging

Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine
- general NRTI side-effects: peripheral neuropathy
- zidovudine: anaemia, myopathy, black nails
- didanosine: pancreatitis

Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz
- side-effects: P450 enzyme interaction (nevirapine induces), rashes

Protease inhibitors (PI)

- examples: indinavir, nelfinavir, ritonavir, saquinavir
- side-effects: diabetes, hyperlipidaemia, buffalo hump, central obesity, P450 enzyme inhibition
- indinavir: renal stones, asymptomatic hyperbilirubinaemia
- ritonavir: a potent inhibitor of the P450 system

Which one of the following is least recognised as a side-effect of sildenafil?

<input type="radio"/>	A. Blue discolouration of vision
<input type="radio"/>	B. Abnormal liver function tests
<input type="radio"/>	C. Flushing
<input type="radio"/>	D. Nasal congestion
<input type="radio"/>	E. Non-arteritic anterior ischaemic optic neuropathy

Next question

## Sildenafil

Sildenafil is a phosphodiesterase type V inhibitor used in the treatment of impotence

### Contraindications

- patients taking nitrates and related drugs such as nicorandil
- hypotension
- recent stroke or myocardial infarction
- non-arteritic anterior ischaemic optic neuropathy

### Side-effects

- visual disturbances e.g. blue discolouration, non-arteritic anterior ischaemic neuropathy
- nasal congestion
- flushing
- gastrointestinal side-effects
- headache

Which of the following drugs is least likely to cause cholestasis?

<input type="radio"/>	A. Erythromycin
<input type="radio"/>	B. Nitrofurantoin
<input type="radio"/>	C. Methyldopa
<input type="radio"/>	D. Gliclazide
<input type="radio"/>	E. Oral contraceptive pill

### Drug-induced liver disease

Drug-induced liver disease is generally divided into hepatocellular, cholestatic or mixed. There is however considerable overlap, with some drugs causing a range of changes to the liver

The following drugs tend to cause a hepatocellular picture:

- paracetamol
- sodium valproate, phenytoin
- MAOIs
- halothane
- anti-tuberculosis: isoniazid, rifampicin, pyrazinamide
- statins
- alcohol
- amiodarone
- methyldopa

The following drugs tend to cause cholestasis (+/- hepatitis):

- oral contraceptive pill
- antibiotics: flucloxacillin, co-amoxiclav, erythromycin\*, nitrofurantoin
- anabolic steroids, testosterone
- phenothiazines: chlorpromazine, prochlorperazine
- sulphonylureas
- fibrates
- rare reported causes: nifedipine

Liver cirrhosis

- methotrexate
- methyldopa
- amiodarone

\*risk may be reduced with erythromycin stearate



A 70-year-old woman is reviewed. She sustained a fracture of her wrist one year ago, following which a DEXA scan was performed. This showed a T-score of -2.8 SD. Calcium and vitamin D supplementation was started along with oral alendronate. This however was stopped due to oesophagitis. In accordance with NICE guidelines, what is the most suitable next management step?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Start hormone replacement therapy |
| <input type="radio"/> | B. Start raloxifene                  |
| <input type="radio"/> | C. Start teriparatide                |
| <input type="radio"/> | D. Switch to risedronate             |
| <input type="radio"/> | E. Refer for hip protectors          |

[Next question](#)

The 2008 NICE guidelines suggest switching to risedronate or etidronate in patients unable to tolerate alendronate

### Osteoporosis: secondary prevention

NICE guidelines were updated in 2008 on the secondary prevention of osteoporotic fractures in postmenopausal women.

Key points include

- treatment is indicated following osteoporotic fragility fractures in postmenopausal women who are confirmed to have osteoporosis (a T-score of - 2.5 SD or below). In women aged 75 years or older, a DEXA scan may not be required 'if the responsible clinician considers it to be clinically inappropriate or unfeasible'
- vitamin D and calcium supplementation should be offered to all women unless the clinician is confident they have adequate calcium intake and are vitamin D replete
- alendronate is first-line
- around 25% of patients cannot tolerate alendronate, usually due to upper gastrointestinal problems. These patients should be offered risedronate or etidronate (see treatment criteria below)
- strontium ranelate and raloxifene are recommended if patients cannot tolerate bisphosphonates (see treatment criteria below)

### Treatment criteria for patients not taking alendronate

Unfortunately, a number of complicated treatment cut-off tables have been produced in the latest guidelines for patients who do not tolerate alendronate

Risk factors (for use in the tables below)

- parental history of hip fracture

- alcohol intake of 4 or more units per day
- rheumatoid arthritis

T-scores (SD) at (or below) which risedronate or etidronate is recommended when alendronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50-54	Not indicated	- 3.0	- 2.5
55-59	- 3.0	- 3.0	- 2.5
60-64	- 3.0	- 3.0	- 2.5
65-69	- 3.0	- 2.5	- 2.5
70 or older	- 2.5	- 2.5	- 2.5

T-scores (SD) at (or below) which strontium ranelate or raloxifene is recommended when alendronate and either risedronate or etidronate cannot be taken

Age (years)	No risk factors	1 risk factor	2 risk factors
50-54	Not indicated	- 3.5	- 3.5
55-59	- 4.0	- 3.5	- 3.5
60-64	- 4.0	- 3.5	- 3.5
65-69	- 4.0	- 3.5	- 3.0
70-74	- 3.0	- 3.0	- 2.5
75 or older	- 3.0	- 2.5	- 2.5

## Supplementary notes on treatment

### Bisphosphonates

- alendronate, risedronate and etidronate are all licensed for the prevention and treatment of post-menopausal and glucocorticoid-induced osteoporosis
- all three have been shown to reduce the risk of both vertebral and non-vertebral fractures although alendronate, risedronate may be superior to etidronate in preventing hip fractures
- ibandronate is a once-monthly oral bisphosphonate

### Vitamin D and calcium

- poor evidence base to suggest reduced fracture rates in the general population at risk of osteoporotic fractures - may reduce rates in frail, housebound patients

#### Raloxifene - selective oestrogen receptor modulator (SERM)

- has been shown to prevent bone loss and to reduce the risk of vertebral fractures, but has not yet been shown to reduce the risk of non-vertebral fractures
- has been shown to increase bone density in the spine and proximal femur
- may worsen menopausal symptoms
- increased risk of thromboembolic events
- may decrease risk of breast cancer

#### Strontium ranelate

- 'dual action bone agent' - increases deposition of new bone by osteoblasts and reduces the resorption of bone by osteoclasts
- strong evidence base, may be second-line treatment in near future
- increased risk of thromboembolic events

#### Teriparatide

- recombinant form of parathyroid hormone
- very effective at increasing bone mineral density but role in the management of osteoporosis yet to be clearly defined

#### Hormone replacement therapy

- has been shown to reduce the incidence of vertebral fracture and non-vertebral fractures
- due to concerns about increased rates of cardiovascular disease and breast cancer it is no longer recommended for primary or secondary prevention of osteoporosis unless the woman is suffering from vasomotor symptoms

#### Hip protectors

- evidence to suggest significantly reduce hip fractures in nursing home patients
- compliance is a problem

#### Falls risk assessment

- no evidence to suggest reduced fracture rates
- however, do reduce rate of falls and should be considered in management of high risk patients

A 55-year-old man presents with multiple erythematous target lesions two days after starting a new medication. Which one of the following drugs is most likely to have been started?

<input type="radio"/>	A. Levetiracetam
<input type="radio"/>	B. Olanzapine
<input type="radio"/>	C. Carbamazepine
<input type="radio"/>	D. Fluoxetine
<input type="radio"/>	E. Diazepam

[Next question](#)

This patient appears to have erythema multiforme which is a known complication of carbamazepine use

### Erythema multiforme

#### Features

- target lesions
- initially seen on the back of the hands / feet before spreading to the torso
- upper limbs are more commonly affected than the lower limbs
- pruritus is occasionally seen and is usually mild

If symptoms are severe and involve blistering and mucosal involvement the term Stevens-Johnson syndrome is used.

#### Causes

- viruses: herpes simplex virus (the most common cause), Orf\*
- idiopathic
- bacteria: *Mycoplasma*, *Streptococcus*
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill, nevirapine
- connective tissue disease e.g. Systemic lupus erythematosus
- sarcoidosis
- malignancy

\*Orf is a skin disease of sheep and goats caused by a parapox virus

Which one of the following drugs is least associated with pancytopenia?

<input type="radio"/>	A. Carbamazepine
<input type="radio"/>	B. Carbimazole
<input type="radio"/>	C. Lithium
<input type="radio"/>	D. Gold
<input type="radio"/>	E. Chloramphenicol

Next question

Lithium is not commonly associated with pancytopenia

### Drug-induced pancytopenia

Drug causes of pancytopenia

- cytotoxics
- antibiotics: trimethoprim, chloramphenicol
- anti-rheumatoid: gold, penicillamine
- carbimazole\*
- anti-epileptics: carbamazepine
- sulphonylureas: tolbutamide

\*causes both agranulocytosis and pancytopenia

Each of the following are true regarding tricyclic overdose, except:

<input type="radio"/>	A. Anticholinergic features are prominent early on
<input type="radio"/>	B. Metabolic acidosis is a common complication
<input type="radio"/>	C. ECG changes include prolongation of the QT interval
<input type="radio"/>	D. Dialysis is indicated in severe toxicity
<input type="radio"/>	E. QRS duration > 160ms is associated with ventricular arrhythmias

### Tricyclic overdose

Overdose of tricyclic antidepressants is a common presentation to emergency departments. Amitriptyline and dosulepin (dothiepin) are particularly dangerous in overdose.

Early features relate to anticholinergic properties: dry mouth, dilated pupils, agitation, sinus tachycardia, blurred vision.

Features of severe poisoning include:

- arrhythmias
- seizures
- metabolic acidosis
- coma

ECG changes include:

- sinus tachycardia
- widening of QRS
- prolongation of QT interval

Widening of QRS > 100ms is associated with an increased risk of seizures whilst QRS > 160ms is associated with ventricular arrhythmias

### Management

- IV bicarbonate may reduce the risk of seizures and arrhythmias in severe toxicity
- arrhythmias: class 1a (e.g. Quinidine) and class Ic antiarrhythmics (e.g. Flecainide) are contraindicated as they prolong depolarisation. Class III drugs such as amiodarone should also be avoided as they prolong the QT interval. Response to lignocaine is variable and it should be emphasized that correction of acidosis is the first line in management of tricyclic induced arrhythmias
- dialysis is ineffective in removing tricyclics

A 34-year-old man with a history of bipolar disorder is admitted with acute confusion. Lithium levels confirm the clinical diagnosis of lithium toxicity. A decision is made to give sodium bicarbonate. What is the mechanism of action of sodium bicarbonate in this situation?

<input type="radio"/>	A. Reduce gastrointestinal tract absorption
<input type="radio"/>	B. Myocardial stabiliser
<input type="radio"/>	C. Neutralises lithium ions
<input type="radio"/>	D. Central nervous system membrane stabiliser
<input type="radio"/>	E. Increases urine alkalinity

[Next question](#)

Increasing the alkalinity of the urine promotes lithium excretion. The preferred treatment in severe cases would be haemodialysis

### Lithium toxicity

Lithium is mood stabilising drug used most commonly prophylactically in bipolar disorder but also as an adjunct in refractory depression. It has a very narrow therapeutic range (0.4-1.0 mmol/L) and a long plasma half-life being excreted primarily by the kidneys. Lithium toxicity generally occurs following concentrations > 1.5 mmol/L.

Toxicity may be precipitated by dehydration, renal failure, diuretics (especially bendroflumethiazide) or ACE inhibitors

#### Features of toxicity

- coarse tremor (a fine tremor is seen in therapeutic levels)
- acute confusion
- seizure
- coma

#### Management

- mild-moderate toxicity may respond to volume resuscitation with normal saline
- haemodialysis may be needed in severe toxicity
- sodium bicarbonate is sometimes used but there is limited evidence to support this. By increasing the alkalinity of the urine it promotes lithium excretion

Which of the following drugs is considered most likely to precipitate an attack of acute intermittent porphyria?

<input type="radio"/>	A. Morphine
<input type="radio"/>	B. Aspirin
<input type="radio"/>	C. Atenolol
<input type="radio"/>	D. Metformin
<input type="radio"/>	E. Oral contraceptive pill

Next question

### Acute intermittent porphyria: drugs

Acute intermittent porphyria (AIP) is an autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40 year olds. AIP is more common in females (5:1)

Drugs which may precipitate attack

- barbiturates
- halothane
- benzodiazepines
- alcohol
- oral contraceptive pill
- sulphonamides

Drugs considered safe to use

- paracetamol
- aspirin
- codeine
- morphine
- chlorpromazine
- beta-blockers
- penicillin
- metformin



You are considering prescribing varenicline to a 45-year-old man who is trying to stop smoking. Which one of the following conditions is most likely to contradict the prescription of varenicline?

<input type="radio"/>	A. Previous or current central nervous system tumour
<input type="radio"/>	B. Past history of deliberate self-harm
<input type="radio"/>	C. Hypertension
<input type="radio"/>	D. Epilepsy
<input type="radio"/>	E. Obesity

[Next question](#)

Varenicline should be used with caution in patients with a history of depression. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline.

### Smoking cessation

NICE released guidance in 2008 on the management of smoking cessation. General points include:

- patients should be offered nicotine replacement therapy (NRT), varenicline or bupropion - NICE state that clinicians should not favour one medication over another
- NRT, varenicline or bupropion should normally be prescribed as part of a commitment to stop smoking on or before a particular date (target stop date)
- prescription of NRT, varenicline or bupropion should be sufficient to last only until 2 weeks after the target stop date. Normally, this will be after 2 weeks of NRT therapy, and 3-4 weeks for varenicline and bupropion, to allow for the different methods of administration and mode of action. Further prescriptions should be given only to people who have demonstrated that their quit attempt is continuing
- if unsuccessful using NRT, varenicline or bupropion, do not offer a repeat prescription within 6 months unless special circumstances have intervened
- do not offer NRT, varenicline or bupropion in any combination

### Nicotine replacement therapy

- adverse effects include nausea & vomiting, headaches and flu-like symptoms
- NICE recommend offering a combination of nicotine patches and another form of NRT (such as gum, inhalator, lozenge or nasal spray) to people who show a high level of dependence on nicotine or who have found single forms of NRT inadequate in the past

### Varenicline

- a nicotinic receptor partial agonist
- should be started 1 week before the patients target date to stop

- the recommended course of treatment is 12 weeks (but patients should be monitored regularly and treatment only continued if not smoking)
- has been shown in studies to be more effective than bupropion
- nausea is the most common adverse effect. Other common problems include headache, insomnia, abnormal dreams
- varenicline should be used with caution in patients with a history of depression or self-harm. There are ongoing studies looking at the risk of suicidal behaviour in patients taking varenicline
- contraindicated in pregnancy and breast feeding

## Bupropion

- a norepinephrine and dopamine reuptake inhibitor, and nicotinic antagonist
- should be started 1 to 2 weeks before the patients target date to stop
- small risk of seizures (1 in 1,000)
- contraindicated in epilepsy, pregnancy and breast feeding. Having an eating disorder is a relative contraindication

Which of the following antibiotics is predominately bacteriostatic?

<input type="radio"/>	A. Metronidazole
<input type="radio"/>	B. Penicillins
<input type="radio"/>	C. Isoniazid
<input type="radio"/>	D. Sulphonamides
<input type="radio"/>	E. Aminoglycosides

Next question

### Antibiotics: bactericidal vs. bacteriostatic

#### Bactericidal antibiotics

- penicillins
- cephalosporins
- aminoglycosides
- nitrofurantoin
- metronidazole
- quinolones
- rifampicin
- isoniazid

#### Bacteriostatic antibiotics

- chloramphenicol
- macrolides
- tetracyclines
- sulphonamides
- trimethoprim

What is the mechanism of action of bivalirudin in acute coronary syndrome?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Activates antithrombin III                |
| <input type="radio"/> | B. Inhibits the production of thromboxane A2 |
| <input type="radio"/> | C. Coronary vasodilator                      |
| <input type="radio"/> | D. Reversible direct thrombin inhibitor      |
| <input type="radio"/> | E. Glycoprotein IIb/IIIa receptor antagonist |

Next question

### Acute coronary syndrome: management

NICE produced guidelines in 2010 on the management of unstable angina and non-ST elevation myocardial infarction (NSTEMI). They advocate managing patients based on the early risk assessment using a recognised scoring system such as GRACE (Global Registry of Acute Cardiac Events) to calculate a predicted 6 month mortality.

All patients should receive

- aspirin 300mg
- nitrates or morphine to relieve chest pain if required

Whilst it is common that non-hypoxic patients receive oxygen therapy there is little evidence to support this approach. The 2008 British Thoracic Society oxygen therapy guidelines advise not giving oxygen unless the patient is hypoxic.

**Antithrombin** treatment. Fondaparinux should be offered to patients who are not at a high risk of bleeding and who are not having angiography within the next 24 hours. If angiography is likely within 24 hours or a patients creatinine is  $> 265 \mu\text{mol/l}$  unfractionated heparin should be given.

**Clopidogrel** 300mg should be given to patients with a predicted 6 month mortality of more than 1.5% or patients who may undergo percutaneous coronary intervention within 24 hours of admission to hospital. Clopidogrel should be continued for 12 months.

Intravenous **glycoprotein IIb/IIIa receptor antagonists** (eptifibatide or tirofiban) should be given to patients who have an intermediate or higher risk of adverse cardiovascular events (predicted 6-month mortality above 3.0%), and who are scheduled to undergo angiography within 96 hours of hospital admission.

**Coronary angiography** should be considered within 96 hours of first admission to hospital to patients who have a predicted 6-month mortality above 3.0%. It should also be performed as soon as possible in patients who are clinically unstable.

The table below summaries the mechanism of action of drugs commonly used in the management of acute coronary syndrome:

<b>Aspirin</b>	Antiplatelet - inhibits the production of thromboxane A <sub>2</sub>
<b>Clopidogrel</b>	Antiplatelet - inhibits ADP binding to its platelet receptor
<b>Enoxaparin</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Fondaparinux</b>	Activates antithrombin III, which in turn potentiates the inhibition of coagulation factors Xa
<b>Bivalirudin</b>	Reversible direct thrombin inhibitor

Which one of the following features is least associated with ecstasy poisoning?

<input type="radio"/>	A. Rhabdomyolysis
<input type="radio"/>	B. Hyperthermia
<input type="radio"/>	C. Ataxia
<input type="radio"/>	D. Hypertension
<input type="radio"/>	E. Hypernatraemia

Next question

Ecstasy is thought to stimulate the production of anti-diuretic hormone. Users of ecstasy also commonly drink too much water in the (mistaken) belief that this will protect them from the adverse effects.

### Ecstasy poisoning

Ecstasy (MDMA, 3,4-Methylenedioxymethamphetamine) use became popular in the 1990's during the emergence of dance music culture

#### Clinical features

- neurological: agitation, anxiety, confusion, ataxia
- cardiovascular: tachycardia, hypertension
- hyponatraemia
- hyperthermia
- rhabdomyolysis

#### Management

- supportive
- dantrolene may be used for hyperthermia if simple measures fail

Which one of the following is least recognised as an adverse effect of phenytoin use?

<input type="radio"/>	A. Megaloblastic anaemia
<input type="radio"/>	B. Peripheral neuropathy
<input type="radio"/>	C. Alopecia
<input type="radio"/>	D. Osteomalacia
<input type="radio"/>	E. Coarsening of facial features

Next question

Phenytoin is associated with hirsutism, rather than alopecia

### Phenytoin

Phenytoin is used to in the management of seizures.

Mechanism of action

- sodium channel blocker, decreasing the sodium influx into neurons which in turn decreases excitability

Phenytoin is associated with a large number of adverse effects. These may be divided into acute, chronic, idiosyncratic and teratogenic

Acute

- initially: vertigo, diplopia, nystagmus, slurred speech, ataxia
- later: confusion, seizures

Chronic

- common: gingival hyperplasia (secondary to increased expression of platelet derived growth factor, PDGF), hirsutism, coarsening of facial features
- megaloblastic anaemia (secondary to altered folate metabolism)
- peripheral neuropathy
- enhanced vitamin D metabolism causing osteomalacia
- lymphadenopathy
- dyskinesia

Idiosyncratic

- fever

- rashes, including severe reactions such as toxic epidermal necrolysis
- hepatitis
- Dupuytren's contracture\*
- aplastic anaemia
- drug-induced lupus

#### Teratogenic

- associated with cleft palate and congenital heart disease

\*although not listed in the BNF



An elderly man is admitted to the acute medical unit with dyspnoea. He is known to have ischaemic heart disease and chronic heart failure (NYHA class III). He develops atrial fibrillation with a fast ventricular response during his admission. Which one of the following drugs is contraindicated?

<input type="radio"/>	A. Amiodarone
<input type="radio"/>	B. Digoxin
<input type="radio"/>	C. Bisoprolol
<input type="radio"/>	D. Flecainide
<input type="radio"/>	E. Warfarin

[Next question](#)

Flecainide is contraindicated in patients with structural heart disease.

### Prescribing in patients with heart failure

The following medications may exacerbate heart failure:

- thiazolidinediones\*: pioglitazone is contraindicated as it causes fluid retention
- verapamil: negative inotropic effect
- NSAIDs\*\*/glucocorticoids: should be used with caution as they cause fluid retention
- class I antiarrhythmics; flecainide (negative inotropic and proarrhythmic effect)

\*pioglitazone is now the only thiazolidinedione on the market

\*\*low-dose aspirin is an exception - many patients will have coexistent cardiovascular disease and the benefits of taking aspirin easily outweigh the risks

Which of the following is true regarding the pathophysiology of paracetamol overdose?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Paracetamol is normally exclusively metabolised by the P450 system                         |
| <input type="radio"/> | B. Paracetamol overdose leads to an excessive build up of mercapturic acid                    |
| <input type="radio"/> | C. Conjugation of paracetamol becomes saturated in overdose                                   |
| <input type="radio"/> | D. Glutathione levels increase following paracetamol overdose leading to hepatocellular death |
| <input type="radio"/> | E. N-acetyl cysteine acts by antagonising glutathione   |

Next question

### Paracetamol overdose: metabolic pathways

The liver normally conjugates paracetamol with glucuronic acid/sulphate. During an overdose the conjugation system becomes saturated leading to oxidation by P450 mixed function oxidases\*. This produces a toxic metabolite (N-acetyl-B-benzoquinone imine)

Normally glutathione acts as a defence mechanism by conjugating with the toxin forming the non-toxic mercapturic acid. If glutathione stores run-out, the toxin forms covalent bonds with cell proteins, denaturing them and leading to cell death. This occurs not only in hepatocytes but also in the renal tubules

N-acetyl cysteine is used in the management of paracetamol overdose as it is a precursor of glutathione and hence can increase hepatic glutathione production

\*this explains why there is a lower threshold for treating patients who take P450 inducing medications e.g. phenytoin or rifampicin

Which one of the following drugs has been associated with an increased risk of atypical stress fractures of the proximal femoral shaft?

<input type="radio"/>	A. Spironolactone
<input type="radio"/>	B. Alendronate
<input type="radio"/>	C. Quetiapine
<input type="radio"/>	D. Venlafaxine
<input type="radio"/>	E. Clopidogrel

[Next question](#)

## Bisphosphonates

Bisphosphonates are analogues of pyrophosphate, a molecule which decreases demineralisation in bone. They inhibit osteoclasts by reducing recruitment and promoting apoptosis

### Clinical uses

- prevention and treatment of osteoporosis
- hypercalcaemia
- Paget's disease
- pain from bone metastases

### Adverse effects

- oesophageal reactions: oesophagitis, oesophageal ulcers (especially alendronate)
- osteonecrosis of the jaw
- increased risk of atypical stress fractures of the proximal femoral shaft in patients taking alendronate

The BNF suggests the following counselling for patients taking oral bisphosphonates

- 'Tablets should be swallowed whole with plenty of water while sitting or standing; to be given on an empty stomach at least 30 minutes before breakfast (or another oral medication); patient should stand or sit upright for at least 30 minutes after taking tablet'

A patient who was commenced on a simvastatin six months ago presents with generalised muscles aches. Which one of the following is not a risk factor for statin-induced myopathy?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Female gender                 |
| <input type="radio"/> | B. Large fall in LDL-cholesterol |
| <input type="radio"/> | C. Low body mass index           |
| <input type="radio"/> | D. Advanced age                  |
| <input type="radio"/> | E. History of diabetes mellitus  |

[Next question](#)

## Statins

Statins inhibit the action of HMG-CoA reductase, the rate-limiting enzyme in hepatic cholesterol synthesis

### Adverse effects

- myopathy: includes myalgia, myositis, rhabdomyolysis and asymptomatic raised creatine kinase. Risks factors for myopathy include advanced age, female sex, low body mass index and presence of multisystem disease such as diabetes mellitus. Myopathy is more common in lipophilic statins (simvastatin, atorvastatin) than relatively hydrophilic statins (rosuvastatin, pravastatin, fluvastatin)
- liver impairment: the 2008 NICE guidelines recommend checking LFTs at baseline, 3 months and 12 months. Treatment should be discontinued if serum transaminase concentrations rise to and persist at 3 times the upper limit of the reference range

### Who should receive a statin?

- all people with established cardiovascular disease (stroke, TIA, ischaemic heart disease, peripheral arterial disease)
- NICE recommend anyone with a 10-year cardiovascular risk  $\geq 20\%$
- the management of blood lipids in type 2 diabetes mellitus (T2DM) has changed slightly. Previously all patients with T2DM  $> 40$ -years-old were prescribed statins. Now patients  $> 40$ -years-old who have no obvious cardiovascular risk (e.g. Non-smoker, not obese, normotensive etc) and have a cardiovascular risk  $< 20\%/10$  years do not need to be given a statin. We suggest reviewing the NICE T2DM guidelines for further information

Statins should be taken at night as this is when the majority of cholesterol synthesis takes place. This is especially true for simvastatin which has a shorter half-life than other statins

Current guidelines for lipid lowering\*

	<b>Total cholesterol (mmol/l)</b>	<b>LDL cholesterol</b>
Joint British Societies	< 4.0	< 2.0
National Service Framework for CHD	< 5.0	< 3.0
SIGN 2007	< 5.0	< 3.0

\*current NICE guidelines do not recommend a target cholesterol in primary prevention

A 35-year-old man with a history of schizophrenia is transferred to the Emergency Department due to an oculogyric crisis. What is the most appropriate treatment?

<input type="radio"/>	A. Selegiline
<input type="radio"/>	B. Haloperidol
<input type="radio"/>	C. Procyclidine
<input type="radio"/>	D. Bromocriptine
<input type="radio"/>	E. Cabergoline

[Next question](#)

Benztropine is also an appropriate treatment

### Antipsychotics

Antipsychotics act as dopamine D2 receptor antagonists, blocking dopaminergic transmission in the mesolimbic pathways. Conventional antipsychotics are associated with problematic extrapyramidal side-effects which has led to the development of atypical antipsychotics such as clozapine

#### Extrapyramidal side-effects

- Parkinsonism
- acute dystonia (e.g. torticollis, oculogyric crisis)
- akathisia (severe restlessness)
- tardive dyskinesia (late onset of choreoathetoid movements, abnormal, involuntary, may occur in 40% of patients, may be irreversible, most common is chewing and pouting of jaw)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:

- increased risk of stroke
- increased risk of venous thromboembolism

#### Other side-effects

- antimuscarinic: dry mouth, blurred vision, urinary retention, constipation
- sedation, weight gain
- raised prolactin: galactorrhoea
- neuroleptic malignant syndrome: pyrexia, muscle stiffness
- reduced seizure threshold (greater with atypicals)

A patient with type 2 diabetes mellitus is started on sitagliptin. What is the mechanism of action of sitagliptin?

- |                                  |   |
|----------------------------------|---|
| <input type="radio"/>            | A. Incretin inhibitor                       |
| <input checked="" type="radio"/> | B. Dipeptidyl peptidase-4 (DPP-4) inhibitor |
| <input type="radio"/>            | C. Alpha-glucosidase inhibitor              |
| <input type="radio"/>            | D. Glucagon inhibitor                       |
| <input type="radio"/>            | E. Glucagon-like peptide-1 (GLP-1) mimetic  |

Next question

Gliptins = Dipeptidyl peptidase-4 (DPP-4) inhibitors

### Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of > 0.5 percentage points in HbA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione



Which one of the following is not a recognised side-effects of dopamine receptor agonists?

<input type="radio"/>	A. Postural hypotension
<input type="radio"/>	B. Daytime somnolence
<input type="radio"/>	C. Galactorrhoea
<input type="radio"/>	D. Nausea
<input type="radio"/>	E. Hallucinations

## Dopamine receptor agonists

### Indications

- Parkinson's disease
- prolactinoma/galactorrhoea
- cyclical breast disease
- acromegaly

Currently accepted practice in the management of patients with Parkinson's disease is to delay treatment until the onset of disabling symptoms and then to introduce a dopamine receptor agonist. If the patient is elderly, L-dopa is sometimes used as an initial treatment

### Overview

- e.g. bromocriptine, ropinirole, cabergoline, apomorphine
- ergot-derived dopamine receptor agonists (bromocriptine, cabergoline, pergolide\*) have been associated with pulmonary, retroperitoneal and cardiac fibrosis. The Committee on Safety of Medicines advice that an ESR, creatinine and chest x-ray should be obtained prior to treatment and patients should be closely monitored

### Adverse effects

- nausea/vomiting
- postural hypotension
- hallucinations
- daytime somnolence

\*pergolide was withdrawn from the US market in March 2007 due to concern regarding increased incidence of valvular dysfunction

A 64-year-old female with a 30 year history of rheumatoid arthritis is noted to have proteinuria on annual review. Which one of the following drugs is most associated with the development of proteinuria?

<input type="radio"/>	A. Ciclosporin
<input type="radio"/>	B. Sodium aurothiomalate
<input type="radio"/>	C. Methotrexate
<input type="radio"/>	D. Infliximab
<input type="radio"/>	E. Azathioprine

[Next question](#)

Nephrotic syndrome - drug causes: gold, penicillamine

### Nephrotic syndrome: causes

Primary glomerulonephritis accounts for around 80% of cases

- minimal change glomerulonephritis (causes 80% in children, 30% in adults)
- membranous glomerulonephritis
- focal segmental glomerulosclerosis
- membranoproliferative glomerulonephritis

Systemic disease (about 20%)

- diabetes mellitus
- systemic lupus erythematosus
- amyloidosis

Drugs

- gold (sodium aurothiomalate), penicillamine

Others

- congenital
- neoplasia: carcinoma, lymphoma, leukaemia, myeloma
- infection: bacterial endocarditis, hepatitis B, malaria

A 62-year-old woman with a history of recurrent deep vein thrombosis secondary to antiphospholipid syndrome presents for review. She has taken warfarin for the past 7 years, with a target INR of 2.0 - 3.0. Her control is normally very good but her last reading was 1.2. Which one of the following would explain her current INR?

<input type="radio"/>	A. Starting fluoxetine for depression
<input type="radio"/>	B. The formation of lupus anticoagulant autoantibodies
<input type="radio"/>	C. Giving up smoking
<input type="radio"/>	D. Recent rifampicin as she was a contact of a patient with meningococcal meningitis
<input type="radio"/>	E. A course of ciprofloxacin for a urinary tract infection

### P450 enzyme system

Induction usually requires prolonged exposure to the inducing drug, as opposed to P450 inhibitors, where effects are often seen rapidly

Inducers of the P450 system include

- antiepileptics: phenytoin, carbamazepine
- barbiturates: phenobarbitone
- rifampicin
- St John's Wort
- chronic alcohol intake
- griseofulvin
- smoking (affects CYP1A2, reason why smokers require more aminophylline)

Inhibitors of the P450 system include

- antibiotics: ciprofloxacin, erythromycin
- isoniazid
- cimetidine, omeprazole
- amiodarone
- allopurinol
- imidazoles: ketoconazole, fluconazole
- SSRIs: fluoxetine, sertraline
- ritonavir
- sodium valproate
- acute alcohol intake
- quinupristin

A 27-year-old woman is started on risperidone for schizophrenia. Which receptor does risperidone have the highest affinity for?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Dopamine D1 receptor                  |
| <input type="radio"/> | B. Serotonin 5-HT <sub>2A</sub> receptor |
| <input type="radio"/> | C. Alpha-adrenoceptor                    |
| <input type="radio"/> | D. Histamine H <sub>1</sub> receptor     |
| <input type="radio"/> | E. Dopamine D <sub>2</sub> receptor      |

Next question

This question is tough and very small print. Risperidone is an atypical antipsychotic agent that displays 5-HT<sub>2A</sub> receptor antagonism. The receptor affinity (K<sub>i</sub>) values are 0.4 and 3.13 nM for 5-HT<sub>2A</sub> and D<sub>2</sub> receptors respectively

### Atypical antipsychotics

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics

- weight gain
- clozapine is associated with agranulocytosis (see below)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:

- increased risk of stroke (especially olanzapine and risperidone)
- increased risk of venous thromboembolism

Examples of atypical antipsychotics

- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride

Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in

patients resistant to other antipsychotic medication

Adverse effects of clozapine

- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients

Which of the following antibiotics act by inhibiting protein synthesis?

<input type="radio"/>	A. Cephalosporins
<input type="radio"/>	B. Gentamicin
<input type="radio"/>	C. Rifampicin
<input type="radio"/>	D. Trimethoprim
<input type="radio"/>	E. Flucloxacillin

Next question

### Antibiotics: mechanisms of action

The lists below summarise the site of action of the commonly used antibiotics

Inhibit cell wall formation

- penicillins
- cephalosporins

Inhibit protein synthesis

- aminoglycosides (cause misreading of mRNA)
- chloramphenicol
- macrolides (e.g. erythromycin)
- tetracyclines
- fusidic acid

Inhibit DNA synthesis

- quinolones (e.g. ciprofloxacin)
- metronidazole
- sulphonamides
- trimethoprim

Inhibit RNA synthesis

- rifampicin

A 33-year-old woman who is known to have familial hypercholesterolaemia comes for review. She is planning to have children and asks for advice regarding medication as she currently takes atorvastatin 80mg on. What is the most appropriate advice?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Switch to atorvastatin 10mg                 |
| <input type="radio"/> | B. Continue current drug at same dose          |
| <input type="radio"/> | C. Stop atorvastatin before trying to conceive |
| <input type="radio"/> | D. Switch to ezetimibe                         |
| <input type="radio"/> | E. Switch to simvastatin 40mg                  |

[Next question](#)

Statins should be discontinued in women 3 months before conception due to the risk of congenital defects

### Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that is thought to affect around 1 in 500 people. It results in high levels of LDL-cholesterol which, if untreated, may cause early cardiovascular disease (CVD). FH is caused by mutations in the gene which encodes the LDL-receptor protein.

Clinical diagnosis is now based on the **Simon Broome criteria**:

- in adults total cholesterol (TC) > 7.5 mmol/l and LDL-C > 4.9 mmol/l or children TC > 6.7 mmol/l and LDL-C > 4.0 mmol/l, plus:
- for definite FH: tendon xanthoma in patients or 1st or 2nd degree relatives or DNA-based evidence of FH
- for possible FH: family history of myocardial infarction below age 50 years in 2nd degree relative, below age 60 in 1st degree relative, or a family history of raised cholesterol levels

### Management

- the use of CVD risk estimation using standard tables is not appropriate in FH as they do not accurately reflect the risk of CVD
- referral to a specialist lipid clinic is usually required
- the maximum dose of potent statins are usually required
- first-degree relatives have a 50% chance of having the disorder and should therefore be offered screening. This includes children who should be screened by the age of 10 years if there is one affected parent
- statins should be discontinued in women 3 months before conception due to the risk of congenital defects

A patient is prescribed zanamivir (Relenza) for suspected influenza. Which one of the following underlying problems may increase the likelihood of side-effects?

<input type="radio"/>	A. A history of aspirin sensitivity
<input type="radio"/>	B. Epilepsy
<input type="radio"/>	C. Asthma
<input type="radio"/>	D. Renal impairment
<input type="radio"/>	E. Concurrent use with drugs that prolong the QT interval

[Next question](#)

Zanamivir (Relenza) may induce bronchospasm in asthmatics.

## H1N1 influenza pandemic

The 2009 H1N1 influenza (swine flu) outbreak was first observed in Mexico in early 2009. In June 2009, the WHO declared the outbreak to be a pandemic.

### H1N1

The H1N1 virus is a subtype of the influenza A virus and the most common cause of flu in humans. The 2009 pandemic was caused by a new strain of the H1N1 virus.

The following groups are particularly at risk:

- patients with chronic illnesses and those on immunosuppressants
- pregnant women
- young children under 5 years old

### Features

The majority of symptoms are typical of those seen in a flu-like illness:

- fever greater than 38°C
- myalgia
- lethargy
- headache
- rhinitis
- sore throat
- cough
- diarrhoea and vomiting



A minority of patients may go on to develop an acute respiratory distress syndrome which may require ventilatory support.

## **Treatment**

There are two main treatments currently available:

### Oseltamivir (Tamiflu)

- oral medication
- a neuraminidase inhibitor which prevents new viral particles from being released by infected cells
- common side-effects include nausea, vomiting, diarrhoea and headaches

### Zanamivir (Relenza)

- inhaled medication\*
- also a neuraminidase inhibitor
- may induce bronchospasm in asthmatics

\*intravenous preparations are available for patients who are acutely unwell

Which of the following cytotoxic agents is most associated with ototoxicity?

- ☐ A. Vincristine
- ☐ B. Bleomycin
- ☐ C. Cisplatin
- ☐ D. Doxorubicin
- ☐ E. Cyclophosphamide

Next question

### Cytotoxic agents

The table below summarises the mechanism of action and major adverse effects of commonly used cytotoxic agents

Cytotoxic	Mechanism of action	Adverse effects
Vincristine	Inhibits formation of microtubules	Peripheral neuropathy (reversible)
Cisplatin	Causes cross-linking in DNA	Ototoxicity, peripheral neuropathy, hypomagnesaemia
Bleomycin	Degrades preformed DNA	Lung fibrosis
Doxorubicin	Stabilizes DNA-topoisomerase II complex inhibits DNA & RNA synthesis	Cardiomyopathy
Methotrexate	Inhibits dihydrofolate reductase and thymidylate synthesis	Myelosuppression, mucositis, liver fibrosis
Cyclophosphamide	Alkylating agent - causes cross-linking in DNA	Haemorrhagic cystitis, myelosuppression, transitional cell carcinoma
Docetaxel	Prevents microtubule depolymerisation & disassembly, decreasing free tubulin	Neutropaenia
Fluorouracil (5-FU)	Pyrimidine analogue inducing cell cycle arrest and apoptosis (works during S phase)	Myelosuppression, mucositis, dermatitis

Which one of the following side-effects is most associated with ciclosporin use?

<input type="radio"/>	A. Hepatotoxicity
<input type="radio"/>	B. Bone marrow toxicity
<input type="radio"/>	C. Red cell aplasia
<input type="radio"/>	D. Haemorrhagic cystitis
<input type="radio"/>	E. Tinnitus

Next question

### Ciclosporin

Ciclosporin is an immunosuppressant which decreases clonal proliferation of T cells by reducing IL-2 release. It acts by binding to cyclophilin forming a complex which inhibits calcineurin, a phosphatase that activates various transcription factors in T cells

Adverse effects of ciclosporin (note how everything is increased - fluid, BP,  $K^+$ , hair, gums, glucose)

- nephrotoxicity
- hepatotoxicity
- fluid retention
- hypertension
- hyperkalaemia
- hypertrichosis
- gingival hyperplasia
- tremor
- impaired glucose tolerance

Interestingly for an immunosuppressant, ciclosporin is noted by the BNF to be 'virtually non-myelotoxic'.

### Indications

- following organ transplantation
- rheumatoid arthritis
- psoriasis (has a direct effect on keratinocytes as well as modulating T cell function)
- ulcerative colitis
- pure red cell aplasia

A 54-year-old man with hypertension is reviewed in clinic. He complains that over the past two months he has developed ankle swelling. Which one of the following drugs is most likely to be responsible?

- ☐ A. Perindopril
- ☐ B. Amlodipine
- ☐ C. Doxazosin
- ☐ D. Moxonidine
- ☐ E. Losartan

[Next question](#)

Calcium channel blockers - side-effects: headache, flushing, ankle oedema

### Calcium channel blockers

Calcium channel blockers are primarily used in the management of cardiovascular disease. Voltage-gated calcium channels are present in myocardial cells, cells of the conduction system and those of the vascular smooth muscle. The various types of calcium channel blockers have varying effects on these three areas and it is therefore important to differentiate their uses and actions.

Examples	Indications & notes	Side-effects and cautions
<b>Verapamil</b>	Angina, hypertension, arrhythmias  Highly negatively inotropic  Should not be given with beta-blockers as may cause heart block	Heart failure, constipation, hypotension, bradycardia
<b>Diltiazem</b>	Angina, hypertension  Less negatively inotropic than verapamil but caution should still be exercised when patients have heart failure or are taking beta-blockers	Hypotension, bradycardia, heart failure, ankle swelling
<b>Nifedipine, amlodipine, felodipine (dihydropyridines)</b>	Hypertension, angina, Raynaud's  Affects the peripheral vascular smooth muscle more than the myocardium and therefore do not result in worsening of heart failure	Flushing, headache, ankle swelling

Which of the following drugs is most likely to be affected by a patient's acetylator status?

- |                       |                |
|-----------------------|----------------|
| <input type="radio"/> | A. Ethanol     |
| <input type="radio"/> | B. Hydralazine |
| <input type="radio"/> | C. Aspirin     |
| <input type="radio"/> | D. Phenytoin   |
| <input type="radio"/> | E. Verapamil   |

Next question

### Pharmacokinetics: metabolism

Drug metabolism usually involves two types of biochemical reactions - phase I and phase II reactions

- phase I reactions: oxidation, reduction, hydrolysis. Mainly performed by the P450 enzymes but some drugs are metabolised by specific enzymes, for example alcohol dehydrogenase and xanthine oxidase. Products of phase I reactions are typically more active and potentially toxic
- phase II reactions: conjugation. Products are typically inactive and excreted in urine or bile. Glucuronyl, acetyl, methyl, sulphate and other groups are typically involved

The majority of phase I and phase II reactions take place in the liver

### First-pass metabolism

This is a phenomenon where the concentration of a drug is greatly reduced before it reaches the systemic circulation due to hepatic metabolism. As a consequence much larger doses are needed orally than if given by other routes. This effect is seen in many drugs, including:

- aspirin
- isosorbide dinitrate
- glyceryl trinitrate
- lignocaine
- propranolol
- verapamil
- isoprenaline
- testosterone
- hydrocortisone

Questions concerning zero-order kinetics and acetylator status are also common in the exam

## **Zero-order kinetics**

Zero-order kinetics describes metabolism which is independent of the concentration of the reactant. This is due to metabolic pathways becoming saturated resulting in a constant amount of drug being eliminated per unit time. This explains why people may fail a breathalyser test in the morning if they have been drinking the night before

Drugs exhibiting zero-order kinetics

- phenytoin
- salicylates
- heparin
- ethanol

## **Acetylator status**

50% of the UK population are deficient in hepatic N-acetyltransferase

Drugs affected by acetylator status

- isoniazid
- procainamide
- hydralazine
- dapsone
- sulfasalazine

### Question 265 of 265

What is the most appropriate dose of adrenaline to give during a cardiac arrest?

- |    |                  |
|----|------------------|
| A. | 1ml 1:100,000 IV |
| B. | 10ml 1:1,000 IV  |
| C. | 0.5ml 1:1,000 IM |
| D. | 1ml 1:10,000 IV  |
| E. | 10ml 1:10,000 IV |

Recommend Adult Life Support (ALS) adrenaline doses

- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

10ml of the 1:10,000 preparation contains 1mg of adrenaline

### Adrenaline

Adrenaline is a sympathomimetic amine with both alpha and beta adrenergic stimulating properties

Indications

- anaphylaxis
- cardiac arrest

Recommend Adult Life Support (ALS) adrenaline doses

- anaphylaxis: 0.5ml 1:1,000 IM
- cardiac arrest: 10ml 1:10,000 IV or 1ml of 1:1000 IV

Management of accidental injection

- local infiltration of phentolamine

**Question 1 of 402**

Next

A rapid finger-prick blood test to help diagnosis deep vein thrombosis is developed. Comparing the test to current standard techniques a study is done on 1,000 patients:

	DVT present	DVT absent
New test positive	200	100
New test negative	20	680

What is the specificity of the new test?

- ☐ A. 680/880
- ☐ B. 200/220
- ☐ C. 680/780
- ☐ D. 680/700
- ☐ E. 200/300

Next question

Specificity = true negatives / (true negatives + false positives)

= 680 / (680 + 100)

**Screening test statistics**

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	TP / (TP + FN )	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	TN / (TN + FP)	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	TP / (TP + FP)	The chance that the patient has the condition if the diagnostic test is positive
<b>Negative predictive value</b>	TN / (TN + FN)	The chance that the patient does not have the condition if the diagnostic test is negative
<b>Likelihood ratio for a positive test result</b>	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive



<b>Likelihood ratio for a negative test result</b>	$(1 - \text{sensitivity}) / \text{specificity}$	How much the odds of the disease decrease when a test is negative
--	---	---

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Which one of the following would shift the oxygen dissociation curve to the left?

- ☐ A. Carboxyhaemoglobin
- ☐ B. Acidosis
- ☐ C. Raised pCO<sub>2</sub>
- ☐ D. Pyrexia
- ☐ E. Raised 2,3-DPG levels

[Next question](#)

### Oxygen dissociation curve

- shifts **Left** - **Lower** oxygen delivery - **Lower** acidity, temp, 2-3 DPG - also HbF, carboxy/methaemoglobin
- shifts **Right** - **Raised** oxygen delivery - **Raised** acidity, temp, 2-3 DPG

### Oxygen dissociation curve

The oxygen dissociation curve describes the relationship between the percentage of saturated haemoglobin and partial pressure of oxygen in the blood. It is not affected by haemoglobin concentration

#### Basics

- shifts to left = for given oxygen tension there is increased saturation of Hb with oxygen i.e. decreased oxygen delivery to tissues
- shifts to right = for given oxygen tension there is reduced saturation of Hb with oxygen i.e. enhanced oxygen delivery to tissues

#### Shifts to Left = Lower oxygen delivery

- HbF, methaemoglobin, carboxyhaemoglobin
- low [H<sup>+</sup>] (alkali)
- low pCO<sub>2</sub>
- low 2,3-DPG
- low temperature

#### Shifts to Right = Raised oxygen delivery

- raised [H<sup>+</sup>] (acidic)
- raised pCO<sub>2</sub>
- raised 2,3-DPG\*
- raised temperature

\*2,3-diphosphoglycerate

A 22-year-old male with a history of familial adenomatous polyposis (FAP) has a total colectomy. What is the mode of inheritance of FAP?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Uniparental disomy of chromosome 12 |
| <input type="radio"/> | B. Autosomal recessive                 |
| <input type="radio"/> | C. Uniparental disomy of chromosome 14 |
| <input type="radio"/> | D. Autosomal dominant                  |
| <input type="radio"/> | E. X-linked recessive                  |

[Next question](#)

### Colorectal cancer: genetics

It is currently thought there are three types of colon cancer:

- sporadic (95%)
- hereditary non-polyposis colorectal carcinoma (HNPCC, 5%)
- familial adenomatous polyposis (FAP, <1%)

Studies have shown that sporadic colon cancer may be due to a series of genetic mutations. For example, more than half of colon cancers show allelic loss of the APC gene. It is believed a further series of gene abnormalities e.g. activation of the K-ras oncogene, deletion of p53 and DCC tumour suppressor genes lead to invasive carcinoma

HNPCC, an autosomal dominant condition, is the most common form of inherited colon cancer. Around 90% of patients develop cancers, often of the proximal colon, which are usually poorly differentiated and highly aggressive. Currently seven mutations have been identified, which affect genes involved in DNA mismatch repair leading to microsatellite instability. The most common genes involved are:

- MSH2 (60% of cases)
- MLH1 (30%)

The Amsterdam criteria are sometimes used to aid diagnosis:

- at least 3 family members with colon cancer
- the cases span at least two generations
- at least one case diagnosed before the age of 50 years

FAP is a rare autosomal dominant condition which leads to the formation of hundreds of polyps by the age of 30-

40 years. Patients inevitably develop carcinoma. It is due to a mutation in a tumour suppressor gene called adenomatous polyposis coli gene (APC), located on chromosome 5. Genetic testing can be done by analysing DNA from a patient's white blood cells. Patients generally have a total colectomy with ileo-anal pouch formation in their twenties.

Patients with FAP are also at risk from duodenal tumours. A variant of FAP called Gardner's syndrome can also feature osteomas of the skull and mandible, retinal pigmentation, thyroid carcinoma and epidermoid cysts on the skin

Which one of the following diseases is most strongly associated with HLA antigen DR4?

- |                                  |                           |
|----------------------------------|---------------------------|
| <input type="radio"/>            | A. Ankylosing spondylitis |
| <input type="radio"/>            | B. Behcet's disease       |
| <input type="radio"/>            | C. Reiter's syndrome      |
| <input checked="" type="radio"/> | D. Rheumatoid arthritis   |
| <input type="radio"/>            | E. Coeliac disease        |

Next question

#### Rheumatoid arthritis - HLA DR4

Around 70% of patients with rheumatoid arthritis are HLA-DR4. Patients with Felty's syndrome (a triad of rheumatoid arthritis, splenomegaly and neutropaenia) are even more strongly associated with 90% being HLA-DR4

#### HLA associations

HLA antigens are encoded for by genes on chromosome 6. HLA A, B and C are class I antigens whilst DP, DQ, DR are class II antigens. Questions are often based around which diseases have strong HLA associations. The most important associations are listed below:

##### HLA-A3

- haemochromatosis

##### HLA-B5

- Behcet's disease

##### HLA-B27

- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

##### HLA-DQ2/DQ8

- coeliac disease

## HLA-DR2

- narcolepsy
- Goodpasture's

## HLA-DR3

- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

## HLA-DR4

- type 1 diabetes mellitus\*
- rheumatoid arthritis

\*type 1 diabetes mellitus is associated with HLA-DR3 but is more strongly associated with HLA-DR4.

Which one of the following causes of primary immunodeficiency is a T-cell disorder?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Chediak-Higashi syndrome         |
| <input type="radio"/> | B. Chronic granulomatous disease    |
| <input type="radio"/> | C. Common variable immunodeficiency |
| <input type="radio"/> | D. DiGeorge syndrome                |
| <input type="radio"/> | E. Wiskott-Aldrich syndrome         |

Next question

DiGeorge syndrome - a T-cell disorder

DiGeorge syndrome is a primary immunodeficiency disorder caused by T-cell deficiency and dysfunction. It is an example of a microdeletion syndrome. Patients are consequently at increased risk of viral and fungal infections.

### Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

#### Neutrophil disorders

- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

#### B-cell disorders

- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

#### T-cell disorders

- DiGeorge syndrome

#### Combined B- and T-cell disorders

- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome

**Question 6 of 402**

Next

A 60-year-old woman with a history of hypothyroidism and inflammatory arthritis is admitted after slipping on ice and falling over. Some routine blood tests are performed:

Na <sup>+</sup>	141 mmol/l
K <sup>+</sup>	2.9 mmol/l
Chloride	114 mmol/l
Bicarbonate	16 mmol/l
Urea	5.2 mmol/l
Creatinine	75 µmol/l

Which one of the following is most likely to explain these results?

- ☐ A. Renal tubular acidosis (type 1)
- ☐ B. Diabetic ketoacidosis
- ☐ C. Renal tubular acidosis (type 4)
- ☐ D. Aspirin overdose
- ☐ E. Conn's syndrome

Next question

Renal tubular acidosis causes a normal anion gap

The low bicarbonate suggests an acidosis. The anion gap is however normal,  $(141 + 2.9) - (114 + 16) = 13.9$  mmol/l. The different diagnosis is therefore causes of a metabolic acidosis with a normal anion gap.

Aspirin and diabetic ketoacidosis causes a metabolic acidosis associated with a raised anion gap. Conn's syndrome would explain the hypokalaemia but it does not cause a metabolic acidosis.

Renal tubular acidosis type 4 is associated with hyperkalaemia. The correct answer is therefore renal tubular acidosis type 1, which is likely to be secondary to this patient's inflammatory arthritis.

**Metabolic acidosis**

Metabolic acidosis is commonly classified according to the anion gap. This can be calculated by:  $(\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-)$ . If a question supplies the chloride level then this is often a clue that the anion gap should be calculated. The normal range = 10-18 mmol/L

Normal anion gap ( = hyperchloraemic metabolic acidosis)

- gastrointestinal bicarbonate loss: diarrhoea, ureterosigmoidostomy, fistula



- renal tubular acidosis
- drugs: e.g. acetazolamide
- ammonium chloride injection
- Addison's disease

#### Raised anion gap

- lactate: shock, hypoxia
- ketones: diabetic ketoacidosis, alcohol
- urate: renal failure
- acid poisoning: salicylates, methanol

Metabolic acidosis secondary to high lactate levels may be subdivided into two types:

- lactic acidosis type A: shock, hypoxia, burns
- lactic acidosis type B: metformin

**Question 7 of 402**

Next

A 12-year-old girl develops facial swelling and an erythematous itchy rash shortly after being administered the first dose of the HPV vaccine. On arrival the paramedics note a bilateral expiratory wheeze and blood pressure of 80/50 mmHg. In the Gell and Coombs classification of hypersensitivity reactions this is an example of a:

- |                       |                      |
|-----------------------|----------------------|
| <input type="radio"/> | A. Type I reaction   |
| <input type="radio"/> | B. Type II reaction  |
| <input type="radio"/> | C. Type III reaction |
| <input type="radio"/> | D. Type IV reaction  |
| <input type="radio"/> | E. Type V reaction   |

Next question

Anaphylaxis = type I hypersensitivity reaction

**Hypersensitivity**

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

**Type I - Anaphylactic**

- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

**Type II - Cell bound**

- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

**Type III - Immune complex**

- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

**Type IV - Delayed hypersensitivity**

- T cell mediated

- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity

- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

**Question 8 of 402**

Next

A 64-year-old female with a history of rheumatoid arthritis presents with increased difficulty in walking. On examination there is weakness of ankle dorsiflexion and of the extensor hallucis longus associated with loss of sensation on the lateral aspect of the lower leg. What is the most likely diagnosis?

<input type="radio"/>	A. Tibial nerve palsy
<input type="radio"/>	B. Obturator nerve palsy
<input type="radio"/>	C. Common peroneal nerve palsy
<input type="radio"/>	D. Lateral cutaneous nerve palsy
<input type="radio"/>	E. Pudendal nerve palsy

Next question

**Common peroneal nerve lesion**

The sciatic nerve divides into the tibial and common peroneal nerves. Injury often occurs at the neck of the fibula

The most characteristic feature of a common peroneal nerve lesion is foot drop

Other features include:

- weakness of foot dorsiflexion
- weakness of foot eversion
- weakness of extensor hallucis longus
- sensory loss over the dorsum of the foot and the lower lateral part of the leg
- wasting of the anterior tibial and peroneal muscles

A study looks at the use of bisphosphonates in controlling the pain associated with bone metastases. One hundred and twenty patients (120) are enrolled in the study, 40 of whom are given conventional treatment with NSAIDs and radiotherapy. Of the 80 patients who were given bisphosphonates, 40 received significant pain relief.

What is the odds of patient with bone metastases receiving significant pain relief from bisphosphonates?

<input type="radio"/>	A.	0.33
<input type="radio"/>	B.	3
<input type="radio"/>	C.	2
<input type="radio"/>	D.	1
<input type="radio"/>	E.	0.5

Next question

The question is limited to the 80 patients who've been given bisphosphonates. Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome.

40 of the 80 patients received significant pain relief

It can therefore be inferred that 40 of the 80 patients did not receive significant pain relief.

Therefore the odds are  $40 / 40 = 1$

### Odds and odds ratio

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome. The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control.

Odds ratios are the usual reported measure in case-control studies. It approximates to relative risk if the outcome of interest is rare.

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Achieved = 50% pain relief
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol =  $40 / 20 = 2$

The odds of achieving significant pain relief with placebo =  $30 / 60 = 0.5$

Therefore the odds ratio =  $2 / 0.5 = 4$

As part of a research project you are trying to ascertain whether the use of dummies in infants is linked to sudden infant death syndrome. What is the most appropriate form of study design?

- ☐ A. Randomised controlled trial
- ☐ B. Cross-over trial
- ☐ C. Cross-sectional survey
- ☐ D. Case-control study
- ☐ E. Cohort study

[Next question](#)

As sudden infant death syndrome is relatively rare a case-control design is more appropriate than a cohort study.

### Study design

The following table highlights the main features of the main types of study:

<b>Randomised controlled trial</b>	<p>Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo)</p> <p>Practical or ethical problems may limit use</p>
<b>Cohort study</b>	<p>Observational and prospective. Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome.</p> <p>The usual outcome measure is the relative risk.</p> <p>Examples include Framingham Heart Study</p>
<b>Case-control study</b>	<p>Observational and retrospective. Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition.</p> <p>The usual outcome measure is the odds ratio.</p> <p>Inexpensive, produce quick results Useful for studying rare conditions Prone to confounding</p>
<b>Cross-sectional survey</b>	<p>Provide a 'snapshot', sometimes called prevalence studies</p> <p>Provide weak evidence of cause and effect</p>

Which of the following is deficient in patients with hereditary angioedema?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. C1-INH                              |
| <input type="radio"/> | B. C3                                  |
| <input type="radio"/> | C. Heat shock protein type 1           |
| <input type="radio"/> | D. C6                                  |
| <input type="radio"/> | E. Histamine degradation protein (HDP) |

Next question

Hereditary angioedema - C1-INH deficiency

### Hereditary angioedema

Hereditary angioedema is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

#### Investigation

- C1-INH level is low during an attack
- low C2 and C4 levels are seen, even between attacks. Serum C4 is the most reliable and widely used screening tool

#### Symptoms

- attacks may be preceded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

#### Management

- acute: IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help

Patients with deficiencies of which one of the following complement proteins are most predisposed to disseminated meningococcal infection?

<input type="radio"/>	A. C1
<input type="radio"/>	B. C2
<input type="radio"/>	C. C3
<input type="radio"/>	D. C4
<input type="radio"/>	E. C5

Next question

Whilst C3 deficiency is associated with recurrent bacterial infections, C5 deficiency is more characteristically associated with disseminated meningococcal infection

### Complement deficiencies

Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body. Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency

- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)

- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency

- causes recurrent bacterial infections

C5 deficiency

- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency

- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection



Which of the following conditions is inherited in an autosomal recessive fashion?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Hypokalaemic periodic paralysis |
| <input type="radio"/> | B. Adult polycystic disease        |
| <input type="radio"/> | C. Huntington's disease            |
| <input type="radio"/> | D. Friedreich's ataxia             |
| <input type="radio"/> | E. Ehlers-Danlos syndrome          |

Next question

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

### Autosomal recessive conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal recessive:

- Albinism
- Ataxia telangiectasia
- Congenital adrenal hyperplasia
- Cystic fibrosis
- Cystinuria
- Familial Mediterranean Fever
- Fanconi anaemia
- Friedreich's ataxia
- Gilbert's syndrome\*
- Glycogen storage disease
- Haemochromatosis
- Homocystinuria
- Lipid storage disease: Tay-Sach's, Gaucher, Niemann-Pick
- Mucopolysaccharidoses: Hurler's

- PKU
- Sickle cell anaemia
- Thalassaemias
- Wilson's disease

\*this is still a matter of debate and many textbooks will list Gilbert's as autosomal dominant

Which one of the following occurs during reverse transcriptase polymerase chain reaction?

- |                                  |                                  |
|----------------------------------|----------------------------------|
| <input type="radio"/>            | A. Proteins are converted to DNA |
| <input type="radio"/>            | B. DNA is converted to RNA       |
| <input type="radio"/>            | C. Used to amplify DNA           |
| <input checked="" type="radio"/> | D. RNA is converted to DNA       |
| <input type="radio"/>            | E. Proteins are converted to RNA |

Next question

## PCR

Polymerase chain reaction (PCR) is a molecular genetic investigation technique. The main advantage of PCR is its sensitivity: only one strand of sample DNA is needed to detect a particular DNA sequence. It now has many uses including prenatal diagnosis, detection of mutated oncogenes and diagnosis of infections. PCR is also extensively used in forensics. Prior to the procedure it is necessary to have two DNA oligonucleotide primers. These are complimentary to specific DNA sequences at either end of the target DNA

Initial prep

- sample of DNA is added to test tube along with two DNA primers
- a thermostable DNA polymerase (Taq) is added

The following cycle then takes place

- mixture is heated to almost boiling point causing denaturing (uncoiling) of DNA
- mixture is the allowed to cool: complimentary strands of DNA pair up, as there is an excess of the primer sequences they pair with DNA preferentially

The above cycle is then repeated, with the amount of DNA doubling each time

Reverse transcriptase PCR

- used to amplify RNA
- RNA is converted to DNA by reverse transcriptase
- gene expression in the form of mRNA (rather than the actually DNA sequence) can therefore be analyzed

Which of the following is true regarding rheumatoid factor?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. It is usually an IgM molecule reacting against patient's own IgG      |
| <input type="radio"/> | B. High titres are not associated with severe disease                    |
| <input type="radio"/> | C. Rose-Waaler test involves agglutination of IgG coated latex particles |
| <input type="radio"/> | D. 80% of SLE patients are RF positive                                   |
| <input type="radio"/> | E. 50% of patients with Sjogren's syndrome are RF positive               |

Next question

Rheumatoid factor is an IgM antibody against IgG

### Rheumatoid factor

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG

RF can be detected by either

- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:

- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy

**Question 16 of 402**

Next

A 19-year-old female with a history of anorexia nervosa is admitted to hospital. Her BMI has dropped to 16. She has agreed to be fed by nasogastric tube. Which one of the following electrolyte disturbances is most likely to occur?

<input type="radio"/>	A. Hyperkalaemia
<input type="radio"/>	B. Hypocalcaemia
<input type="radio"/>	C. Metabolic acidosis
<input checked="" type="radio"/>	D. Hypophosphataemia
<input type="radio"/>	E. Hypermagnesiumemia

Next question

Refeeding syndrome causes hypophosphataemia

This patient is at risk of refeeding syndrome, which can lead to profound hypophosphataemia

**Hypophosphataemia****Causes**

- alcohol excess
- acute liver failure
- diabetic ketoacidosis
- refeeding syndrome
- primary hyperparathyroidism
- osteomalacia

**Consequences**

- red blood cell haemolysis
- white blood cell and platelet dysfunction
- muscle weakness and rhabdomyolysis
- central nervous system dysfunction

Which one of the following statements regarding gastrin is true?

- ☐ A. Secreted by D cells in the stomach
- ☐ B. Secretion is inhibited by high antral pH
- ☐ C. Reduces acid secretion in the stomach
- ☐ D. Increases gastric motility
- ☐ E. Distension of the stomach inhibits secretion

Next question

### Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
<b>Gastrin</b>	G cells in antrum of the stomach	Distension of stomach, vagus nerves (mediated by gastrin-releasing peptide), luminal peptides/amino acids Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
<b>CCK</b>	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
<b>Secretin</b>	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
<b>VIP</b>	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid secretion
<b>Somatostatin</b>	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production

**Question 18 of 402**

Next

A case-control study is designed to investigate whether being exposed to passive smoking as a child is a risk factor for asthma. Two hundred patients with asthma are recruited. Of these 200, 40 report either one or both parents smoking in the house when they were a child. A further 200 controls who do not have asthma are recruited. Of these people 20 report that one or both parents smoked in the house. What is the odds ratio of asthmatics having been exposed to passive smoking as a child?

- ☐ A. 2.25
- ☐ B. 0.66
- ☐ C. 0.5
- ☐ D. 1.5
- ☐ E. 4

Next question

Odds - remember a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome

NOT a ratio of the number of people who incur a particular outcome to the total number of people

The odds of asthmatics being exposed to passive smoking is  $40 / 160 = 1 / 4$

The odds of the controls being exposed to passive smoking is  $20 / 180 = 1 / 9$

The odds ratio is therefore  $1/4 / 1/9 = 9/4 = 2.25$

**Odds and odds ratio**

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome. The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control.

Odds ratios are the usual reported measure in case-control studies. It approximates to relative risk if the outcome of interest is rare.

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Achieved = 50% pain relief
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol =  $40 / 20 = 2$

The odds of achieving significant pain relief with placebo =  $30 / 60 = 0.5$

Therefore the odds ratio =  $2 / 0.5 = 4$



A randomised controlled trial compares two drugs used in the initial management of rheumatoid arthritis. After being assigned to the randomised groups a number of patients drop out due to adverse effects of the medication. How should the data be analysed?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Recruit more patients  |
| <input type="radio"/> | B. For each patient who drops out, remove a patient from the other randomised group |
| <input type="radio"/> | C. Include the patients who drop out in the final data set                          |
| <input type="radio"/> | D. Remove patients who drop out from final data set                                 |
| <input type="radio"/> | E. Abandon the trial if more than 5% of patients drop out                           |

[Next question](#)

### Intention to treat analysis

Intention to treat analysis is a method of analysis for randomized controlled trials in which all patients randomly assigned to one of the treatments are analysed together, regardless of whether or not they completed or received that treatment

Intention to treat analysis is done to avoid the effects of crossover and drop-out, which may affect the randomization to the treatment groups

Which one of the following would invalidate the use of the Student's t-test when performing a significance test?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Using it with unpaired data  |
| <input type="radio"/> | B. Using it with data that is not normally distributed                                  |
| <input type="radio"/> | C. Using it with data that has a small sample size                                      |
| <input type="radio"/> | D. Using it to test whether the slope of a regression line differs significantly from 0 |
| <input type="radio"/> | E. Using it to test a null hypothesis   |

Next question

Data must be parametric, i.e. follows a normal distribution

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

**Question 21 of 402**

Next

A study is carried out to assess the potential of hip protectors to reduce femoral neck fractures in elderly nursing home patients. The average age of the patients was 82 years. Over a two-year period 800 patients were recruited and assigned randomly either to the hip protector group or standard care group.

**The results:**

Hip protector group: 400 patients - 10 of whom had a femoral neck fracture over the two year period

Control group: 400 patients - 20 of whom had a femoral neck fracture over the two year period

What is the absolute risk reduction?

- |                       |    |       |
|-----------------------|----|-------|
| <input type="radio"/> | A. | 0.025 |
| <input type="radio"/> | B. | 0.05  |
| <input type="radio"/> | C. | 2     |
| <input type="radio"/> | D. | 10    |
| <input type="radio"/> | E. | 0.5   |

Next question

Absolute risk reduction = (Control event rate) - (Experimental event rate)

The absolute risk reduction = CER-EER, where:

Control event rate (CER) = (Number who had particular outcome with the control/ (Total number who had the control)

Experimental event rate (EER) = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

$$\text{CER} = 20 / 400 = 1 / 20 = 0.05$$

$$\text{EER} = 10 / 400 = 1 / 40 = 0.025$$

$$\text{ARR} = \text{CER} - \text{EER} = 0.05 - 0.025 = 0.025$$

**Numbers needed to treat and absolute risk reduction**

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by  $1/(\text{Absolute risk reduction})$  and is rounded to the next highest whole number

Experimental event rate (EER) = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate (CER) = (Number who had particular outcome with the control/ (Total number who had the control)

**Absolute risk reduction = CER-EER or EER-CER?**

The absolute risk reduction (ARR) may be calculated by finding the absolute difference between the control event rate (CER) and the experimental event rate (EER). You will often find both versions of the above listed in different sources. In some ways it doesn't matter which you use as you will end up with the same answer but from a technical point of view:

- if the outcome of the study is undesirable then  $ARR = CER - EER$
- if the outcome of the study is desirable then  $ARR^* = EER - CER$

\*this may be more accurately termed absolute benefit increase, rather than absolute risk reduction

You are reviewing a new study on the benefit of omega-3 fish oils in patients with established ischaemic heart disease. What does the power of the study equate to?

- ☐ A.  $= 1 / p \text{ value}$
- ☐ B.  $= \text{standard deviation} / \text{square root of sample size}$
- ☐ C.  $= 1 - \text{probability of making a type II error}$
- ☐ D.  $= 1 - \text{probability of making a type I error}$
- ☐ E.  $= 1 / \text{probability of making a type I error}$

[Next question](#)

Power = 1 - the probability of a type II error

### Significance tests

A null hypothesis ( $H_0$ ) states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct.

For example:

- 'there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not'

The alternative hypothesis ( $H_1$ ) is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

The **p value** is the probability of obtaining a result by chance at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. It is therefore equal to the chance of making a type I error (see below).

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist, a false positive. This is determined against a preset significance level (termed alpha). As the significance level is determined in advance the chance of making a type I error is not affected by sample size. It is however increased if the number of end-points are increased. For example if a study has 20 end-points it is likely one of these will be reached, just by chance.

- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists, a false negative. The probability of making a type II error is termed beta. It is determined by both sample size and alpha

	Study accepts $H_0$	Study rejects $H_0$
Reality $H_0$		Type 1 error (alpha)
Reality $H_1$	Type 2 error (beta)	Power (1 - beta)

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false, i.e. the probability of detecting a statistically significant difference

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Each one of the following is associated with hyperkalaemia, except:

<input type="radio"/>	A. Rhabdomyolysis
<input type="radio"/>	B. Carbenoxolone
<input type="radio"/>	C. Acute renal failure
<input type="radio"/>	D. Ciclosporin
<input type="radio"/>	E. Addison's

Next question

## Hyperkalaemia

Plasma potassium levels are regulated by a number of factors including aldosterone, acid-base balance and insulin levels. Metabolic acidosis is associated with hyperkalaemia as hydrogen and potassium ions compete with each other for exchange with sodium ions across cell membranes and in the distal tubule. ECG changes seen in hyperkalaemia include tall-tented T waves, small P waves, widened QRS leading to a sinusoidal pattern and asystole

Causes of hyperkalaemia:

- acute renal failure
- drugs\*: potassium sparing diuretics, ACE inhibitors, angiotensin 2 receptor blockers, spironolactone, ciclosporin, heparin\*\*
- metabolic acidosis
- Addison's
- rhabdomyolysis
- massive blood transfusion

Foods that are high in potassium:

- salt substitutes (i.e. Contain potassium rather than sodium)
- bananas, oranges, kiwi fruit, avocado, spinach, tomatoes

\*beta-blockers interfere with potassium transport into cells and can potentially cause hyperkalaemia in renal failure patients - remember beta-agonists, e.g. Salbutamol, are sometimes used as emergency treatment

\*\*both unfractionated and low-molecular weight heparin can cause hyperkalaemia. This is thought to be caused by inhibition of aldosterone secretion

A 35-year-old woman is admitted to the Emergency Department following a deliberate overdose of 50 paracetamol tablets around 10 hours ago. On admission she complains of abdominal pain and lethargy. Her prothrombin time is elevated and arterial blood gases show that she is developing a metabolic acidosis. An urgent transfer to the tertiary liver transplant unit is arranged. What is the main pathological process seen in the hepatocytes of such patients with fulminant hepatitis?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Apoptosis  |
| <input type="radio"/> | B. Fibrosis   |
| <input type="radio"/> | C. Ischaemia  |
| <input type="radio"/> | D. Senescence |
| <input type="radio"/> | E. Necrosis   |

[Next question](#)

In patients such as this one necrosis affects the entire acinus (panacinar necrosis) resulting in liver failure. This is in contrast to the apoptosis seen in patients with mild cases of viral hepatitis, resulting in the possibility of regeneration and recovery of hepatocellular function.

### Acute liver failure

Acute liver failure describes the rapid onset of hepatocellular dysfunction leading to a variety of systemic complications.

#### Causes

- paracetamol overdose
- alcohol
- viral hepatitis (usually A or B)
- acute fatty liver of pregnancy

#### Features\*

- jaundice
- coagulopathy: raised prothrombin time
- hypoalbuminaemia
- hepatic encephalopathy
- renal failure is common ('hepatorenal syndrome')

\*remember that 'liver function tests' do not always accurately reflect the synthetic function of the liver. This is best assessed by looking at the prothrombin time and albumin level.



**Question 25 of 402**

Next

A 72-year-old woman presents with polyuria and polydipsia. Investigations reveal the following:

Fasting glucose	4.5 mmol/l
Calcium	2.88 mmol/l
Phosphate	0.75 mmol/l
Parathyroid hormone	6 pmol/L (normal range = 0.8 - 8.5)

What is the most likely underlying diagnosis?

- ☐ A. Myeloma
- ☐ B. Sarcoidosis
- ☐ C. Primary hyperparathyroidism
- ☐ D. Vitamin D excess
- ☐ E. Osteomalacia

Next question

The PTH level in primary hyperparathyroidism may be normal

Despite a raised calcium level the parathyroid hormone level is inappropriately normal. This points towards a diagnosis of primary hyperparathyroidism and the other causes (such as myeloma) would lead to a suppression of parathyroid hormone

**Primary hyperparathyroidism**

In exams primary hyperparathyroidism is stereotypically seen in elderly females with an unquenchable thirst and an inappropriately normal or raised parathyroid hormone level. It is most commonly due to a solitary adenoma

Causes of primary hyperparathyroidism

- 80%: solitary adenoma
- 15%: hyperplasia
- 4%: multiple adenoma
- 1%: carcinoma

Features - 'bones, stones, abdominal groans and psychic moans'

- polydipsia, polyuria
- peptic ulceration/constipation/pancreatitis
- bone pain/fracture

- renal stones
- depression
- hypertension

#### Associations

- hypertension
- multiple endocrine neoplasia: MEN I and II

#### Investigations

- raised calcium, low phosphate
- PTH may be raised or normal
- technetium-MIBI subtraction scan

#### Treatment

- total parathyroidectomy

The nicotinic acetylcholine receptor is an example of a:

<input type="radio"/>	A. Ligand-gated ion channel
<input type="radio"/>	B. Tyrosine kinase receptor
<input type="radio"/>	C. Guanylate cyclase receptor
<input type="radio"/>	D. G protein-coupled receptor
<input type="radio"/>	E. Intracellular receptor

Next question

## Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

### Ligand-gated ion channel

- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

### Tyrosine kinase receptors

- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

### Guanylate cyclase receptors

- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

### G protein-coupled receptors

- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

**Question 27 of 402**

Next

A 72-year-old woman who takes bendroflumethiazide for hypertension is admitted to the Emergency Department. Admission bloods show the following:

Na <sup>+</sup>	131 mmol/l
K <sup>+</sup>	2.2 mmol/l
Urea	3.1 mmol/l
Creatinine	56 µmol/l
Glucose	4.3 mmol/l

Which one of the following ECG features is most likely to be seen?

- ☐ A. Short PR interval
- ☐ B. Short QT interval
- ☐ C. Flattened P waves
- ☐ D. J waves
- ☐ E. U waves

Next question

Hypokalaemia - U waves on ECG

J waves are seen in hypothermia whilst delta waves are associated with Wolff Parkinson White syndrome.

**ECG: hypokalaemia**

ECG features of hypokalaemia

- U waves
- small or absent T waves (occasionally inversion)
- prolong PR interval
- ST depression
- long QT

The ECG below shows typical U waves. Note also the borderline PR interval.



© Image used on license from [Dr Smith, University of Minnesota](#)



One registered user suggests the following rhyme

- In Hypokalaemia, U have no Pot and no T, but a long PR and a long QT

Vitamin D causes which one of the following:

<input type="radio"/>	A. Increased plasma phosphate
<input type="radio"/>	B. Decreased plasma calcium
<input type="radio"/>	C. Decreased osteoclastic activity
<input type="radio"/>	D. Decreased gut absorption of calcium
<input type="radio"/>	E. Decreased renal tubular absorption of calcium

Next question

Vitamin D increases plasma calcium and plasma phosphate levels by promoting renal tubular absorption and gut absorption of calcium and increasing renal phosphate reabsorption

### Calcium metabolism

The two hormones which primarily control calcium metabolism are:

- parathyroid hormone (PTH)
- 1,25-dihydroxycholecalciferol (calcitriol, the active form of vitamin D)

Other hormones include

- calcitonin: secreted from the C cells of the thyroid gland
- thyroxine
- growth hormone

Actions of parathyroid hormone

- increases plasma calcium, decreases plasma phosphate
- increases renal tubular reabsorption of calcium
- increases osteoclastic activity
- increases renal conversion of 25-hydroxycholecalciferol to 1,25-dihydroxycholecalciferol
- decreases renal phosphate reabsorption

Actions of 1,25-dihydroxycholecalciferol

- increases plasma calcium and plasma phosphate
- increases renal tubular reabsorption and gut absorption of calcium
- increases osteoclastic activity
- increases renal phosphate reabsorption

Which one of the following is least associated with hypercalcaemia?

<input type="radio"/>	A. Sarcoidosis
<input type="radio"/>	B. Primary hyperparathyroidism
<input type="radio"/>	C. Thiazide diuretics
<input type="radio"/>	D. Squamous cell lung cancer
<input type="radio"/>	E. Monoclonal gammopathy of uncertain significance

Next question

One of the key differentiating features between monoclonal gammopathy of uncertain significance (MGUS) and myeloma is the absence of complications such as immune paresis, hypercalcaemia and bone pain

### Hypercalcaemia: causes

The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

- sarcoidosis\*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, calcium containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone\*\*

\*other causes of granulomas may lead to hypercalcaemia e.g. Tuberculosis and histoplasmosis

\*\*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

**Question 30 of 402**

Next

A new test to screen for pulmonary embolism (PE) is used in 100 patients who present to the Emergency Department. The test is positive in 30 of the 40 patients who are proven to have a PE. Of the remaining 60 patients, only 5 have a positive test. What is the sensitivity of the new test?

- ☐ A. 8.33%
- ☐ B. 30%
- ☐ C. 40%
- ☐ D. 66.66%
- ☐ E. 75%

Next question

A contingency table can be constructed from the above data, as shown below:

	PE diagnosed	No PE
Test positive	30	5
Test negative	10	55

The sensitivity is therefore  $30 / (30 + 10) = 75\%$

**Screening test statistics**

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	$TP / (TP + FN)$	Proportion of patients with the condition who have a positive test result
Specificity	$TN / (TN + FP)$	Proportion of patients without the condition who have a negative test result
Positive predictive value	$TP / (TP + FP)$	The chance that the patient has the condition if the diagnostic test is positive
Negative predictive value	$TN / (TN + FN)$	The chance that the patient does not have the condition if the diagnostic test is negative



<b>Likelihood ratio for a positive test result</b>	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
<b>Likelihood ratio for a negative test result</b>	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Which one of the following serum proteins is most likely to increase in a patient with severe pneumococcal pneumonia?

<input type="radio"/>	A. Transferrin
<input type="radio"/>	B. Transthyretin
<input type="radio"/>	C. Ferritin
<input type="radio"/>	D. Albumin
<input type="radio"/>	E. Cortisol binding protein

[Next question](#)

### Acute phase proteins

Acute phase proteins

- CRP
- procalcitonin
- ferritin
- fibrinogen
- alpha-1 antitrypsin
- caeruloplasmin
- serum amyloid A
- serum amyloid P component\*
- haptoglobin
- complement

During the acute phase response the liver decreases the production of other proteins (sometimes referred to as negative acute phase proteins). Examples include:

- albumin
- transthyretin (formerly known as prealbumin)
- transferrin
- retinol binding protein
- cortisol binding protein

\*plays a more significant role in other mammals such as mice

### Question 32 of 402

Next

A 79-year-old man is admitted with congestive cardiac failure. Bloods on admission show:

BNP	354 pg/ml
-----	-----------

Which one of the following would result from elevated BNP levels?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Decreased sodium diuresis                              |
| <input type="radio"/> | B. Vasoconstriction of the coronary arteries              |
| <input type="radio"/> | C. Inhibition of the renin-angiotensin-aldosterone system |
| <input type="radio"/> | D. Vasoconstriction of the pulmonary vessels              |
| <input type="radio"/> | E. Increased sympathetic tone                             |

Next question

BNP - actions:

- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

### B-type natriuretic peptide

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain.

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

Effects of BNP

- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

### Clinical uses of BNP

### Diagnosing patients with acute dyspnoea

- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis
- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure

### Prognosis in patients with chronic heart failure

- initial evidence suggests BNP is an extremely useful marker of prognosis

### Guiding treatment in patients with chronic heart failure

- effective treatment lowers BNP levels

### Screening for cardiac dysfunction

- not currently recommended for population screening

Which one of the following causes of primary immunodeficiency is due to a defect in both B-cell and T-cell function?

<input type="radio"/>	A. Common variable immunodeficiency
<input type="radio"/>	B. Chronic granulomatous disease
<input type="radio"/>	C. Wiskott-Aldrich syndrome
<input type="radio"/>	D. Chediak-Higashi syndrome
<input type="radio"/>	E. Di George syndrome

[Next question](#)

Combined B- and T-cell disorders: SCID WAS ataxic (SCID, Wiskott-Aldrich syndrome, ataxic telangiectasia)

Wiskott-Aldrich syndrome causes primary immunodeficiency due to a combined B- and T-cell dysfunction. It is inherited in a X-linked recessive fashion and is thought to be caused by mutation in the WASP gene. Features include recurrent bacterial infections (e.g. chest), eczema and thrombocytopenia

### Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

Neutrophil disorders

- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

B-cell disorders

- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

T-cell disorders

- DiGeorge syndrome

Combined B- and T-cell disorders

- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome

A 65-year-old man presents with bilateral leg pain that is brought on by walking. His past medical history includes peptic ulcer disease and osteoarthritis. He can typically walk for around 5 minutes before it develops. The pain subsides when he sits down. He has also noticed that leaning forwards or crouching improves the pain.

Musculoskeletal and vascular examination of his lower limbs is unremarkable. What is the most likely diagnosis?

- ☐ A. Inflammatory arachnoiditis
- ☐ B. Peripheral arterial disease
- ☐ C. Raised intracranial pressure
- ☐ D. Spinal stenosis
- ☐ E. Lumbar vertebral crush fracture

This is a classic presentation of spinal stenosis. Whilst peripheral arterial disease is an obvious differential the characteristic relieving factors of the pain and normal vascular examination point away from this diagnosis.

### Lower back pain

Lower back pain (LBP) is one of the most common presentations seen in practice. Whilst the majority of presentations will be of a non-specific muscular nature it is worth keeping in mind possible causes which may need specific treatment.

Red flags for lower back pain

- age < 20 years or > 50 years
- history of previous malignancy
- night pain
- history of trauma
- systemically unwell e.g. weight loss, fever

The table below indicates some specific causes of LBP:

<b>Facet joint</b>	May be acute or chronic Pain worse in the morning and on standing On examination there may be pain over the facets. The pain is typically worse on extension of the back
<b>Spinal stenosis</b>	Usually gradual onset Unilateral or bilateral leg pain (with or without back pain), numbness, and weakness which is worse on walking. Resolves when sits down. Pain may be described as 'aching', 'crawling'. Relieved by sitting down, leaning forwards and crouching down Clinical examination is often normal Requires MRI to confirm diagnosis
<b>Ankylosing spondylitis</b>	Typically a young man who presents with lower back pain and stiffness Stiffness is usually worse in morning and improves with activity Peripheral arthritis (25%, more common if female)
<b>Peripheral arterial disease</b>	Pain on walking, relieved by rest Absent or weak foot pulses and other signs of limb ischaemia Past history may include smoking and other vascular diseases

### Question 35 of 402

Next

You have been asked to investigate the potential benefit of setting up a service to help patients with multiple sclerosis in the local area. What is the most important factor when determining how many resources will be required?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Incidence        |
| <input type="radio"/> | B. Bayesian factor  |
| <input type="radio"/> | C. Prevalence       |
| <input type="radio"/> | D. Denominator data |
| <input type="radio"/> | E. P value          |

Next question

### Incidence and prevalence

These two terms are used to describe the frequency of a condition in a population.

The **incidence** is the number of new cases per population in a given time period.

For example, if condition X has caused 40 new cases over the past 12 months per 1,000 of the population the annual incidence is 0.04 or 4%.

The **prevalence** is the total number of cases per population at a particular point in time.

For example, imagine a questionnaire is sent to 2,500 adults asking them how much they weigh. If from this sample population of 500 of the adults were obese then the prevalence of obesity would be 0.2 or 20%.

### Relationship

- prevalence = incidence \* duration of condition
- in chronic diseases the prevalence is much greater than the incidence
- in acute diseases the prevalence and incidence are similar. For conditions such as the common cold the incidence may be greater than the prevalence

In the Gell and Coombs classification of hypersensitivity reactions scabies is an example of a:

- |                       |                      |
|-----------------------|----------------------|
| <input type="radio"/> | A. Type I reaction   |
| <input type="radio"/> | B. Type II reaction  |
| <input type="radio"/> | C. Type III reaction |
| <input type="radio"/> | D. Type IV reaction  |
| <input type="radio"/> | E. Type V reaction   |

Scabies produces a delayed type IV hypersensitivity reaction approximately one month after infestation. This produces the characteristic intense itching

### Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic

- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound

- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

Type III - Immune complex

- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

Type IV - Delayed hypersensitivity

- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity

- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis



Which one of the following electrolyte disturbances is most associated with the development of a prolonged QT interval on ECG?

<input type="radio"/>	A. Hyponatraemia
<input type="radio"/>	B. Hypocalcaemia
<input type="radio"/>	C. Hyperkalaemia
<input type="radio"/>	D. Hypercalcaemia
<input type="radio"/>	E. Hypophosphataemia

[Next question](#)

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"> <li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li> <li>Romano-Ward syndrome (no deafness)</li> </ul>	<ul style="list-style-type: none"> <li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li> <li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li> <li>methadone</li> <li>chloroquine</li> <li>terfenadine**</li> <li>erythromycin</li> </ul>	<ul style="list-style-type: none"> <li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li> <li>acute myocardial infarction</li> <li>myocarditis</li> <li>hypothermia</li> <li>subarachnoid haemorrhage</li> </ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli
- Long QT3 - events often occur at night or at rest
- sudden cardiac death

## Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

Which one of the following statements regarding mitochondrial inheritance is true?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Friedreich's ataxia is caused by defects in mitochondrial DNA                                |
| <input type="radio"/> | B. There is a 50% chance that the female offspring of an affected male will inherit the disease |
| <input type="radio"/> | C. Affected females cannot pass on the disease  |
| <input type="radio"/> | D. Most cases of spinocerebellar ataxia are caused by defects in mitochondrial DNA              |
| <input type="radio"/> | E. Poor genotype:phenotype correlation  |

Next question

### Mitochondrial diseases

Whilst most DNA is found in the cell nucleus, a small amount of double-stranded DNA is present in the mitochondria. It encodes protein components of the respiratory chain and some special types of RNA

Mitochondrial inheritance has the following characteristics:

- inheritance is only via the maternal line as the sperm contributes no cytoplasm to the zygote
- all children of affected males will not inherit the disease
- all children of affected females will inherit it
- generally encode rare neurological diseases
- poor genotype:phenotype correlation - within a tissue or cell there can be different mitochondrial populations - this is known as heteroplasmy)

Histology

- muscle biopsy classically shows 'red, ragged fibres' due to increased number of mitochondria

Examples include:

- Leber's optic atrophy
- MELAS syndrome: mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes
- MERRF syndrome: myoclonus epilepsy with ragged-red fibres
- Kearns-Sayre syndrome: onset in patients < 20 years old, external ophthalmoplegia, retinitis pigmentosa. Ptosis may be seen
- sensorineural hearing loss

**Question 39 of 402**

Next

A new drug designed to prevent exacerbations of genital herpes undergoes clinical trials. One hundred patients are given the new drug. During a three month period 10 of the patients have an episode of genital herpes. In the control group there are 300 patients who are given a placebo. In this group 50 people have an exacerbation during the same time period. What is the relative risk of having an exacerbation of genital herpes whilst taking the new drug?

- ☐ A. 0.8
- ☐ B. 0.2
- ☐ C. 1.66
- ☒ D. 0.6
- ☐ E. 0.06

Next question

Experimental event rate,  $EER = 10 / 100 = 0.10$

Control event rate,  $CER = 50 / 300 = 0.166$

Therefore the relative risk =  $EER / CER = 0.1 / 0.166 = 0.6$

**Relative risk**

**Relative risk (RR)** is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER). The term relative risk ratio is sometimes used instead of relative risk.

To recap

- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Experienced significant pain relief
Paracetamol	100	60
Placebo	80	20

Experimental event rate,  $EER = 60 / 100 = 0.6$

Control event rate,  $CER = 20 / 80 = 0.25$

Therefore the relative risk ratio =  $EER / CER = 0.6 / 0.25 = 2.4$

If the risk ratio is  $> 1$  then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is  $< 1$  then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

**Relative risk reduction (RRR)** or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate

Using the above data,  $RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140\%$

Which one of the following statements regarding nitric oxide is incorrect?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Promotes platelet aggregation                               |
| <input type="radio"/> | B. Raises intracellular cGMP levels                            |
| <input type="radio"/> | C. An inducible form of NOS is present in macrophages          |
| <input type="radio"/> | D. In sepsis increased levels of NO contribute to septic shock |
| <input type="radio"/> | E. Causes venodilation   |

Next question

Nitric oxide - vasodilation + inhibits platelet aggregation

Nitric oxide inhibits, rather than promotes, platelet aggregation

### Nitric oxide

Previously known as endothelium derived relaxation factor, nitric oxide (NO) has emerged as a molecule which is integral to many physiological and pathological processes. It is formed from L-arginine and oxygen by nitric oxide synthetase (NOS). An inducible form of NOS has been shown to be present in macrophages. Nitric oxide has a very short half-life (seconds), being inactivated by oxygen free radicals

### Effects

- acts on guanylate cyclase leading to raised intracellular cGMP levels and therefore decreasing  $\text{Ca}^{2+}$  levels
- vasodilation, mainly venodilation
- inhibits platelet aggregation

### Clinical relevance

- underproduction of NO is implicated in hypertrophic pyloric stenosis
- lack of NO is thought to promote atherosclerosis
- in sepsis increased levels of NO contribute to septic shock
- organic nitrates (metabolism produces NO) is widely used to treat cardiovascular disease (e.g. angina, heart failure)
- sildenafil is thought to potentiate the action of NO on penile smooth muscle and is used in the treatment of erectile dysfunctions

Which of the following statements is true regarding hyponatraemia?

<input type="radio"/>	A. In a dehydrated patient with urinary sodium < 20mmol/L it may be due to the diuretic stage of renal failure
<input type="radio"/>	B. SIADH typically leads to urine osmolality of < 500 mmol/kg
<input type="radio"/>	C. Hyperlipidaemia may cause pseudohyponatraemia
<input type="radio"/>	D. Cardiac failure and liver cirrhosis may lead to primary hyperaldosteronism
<input type="radio"/>	E. It is known to cause a long QT interval

Next question

## Hyponatraemia

Hyponatraemia may be caused by water excess or sodium depletion. Causes of pseudohyponatraemia include hyperlipidaemia (increase in serum volume) or a taking blood from a drip arm. Urinary sodium and osmolality levels aid making a diagnosis

### Urinary sodium > 20 mmol/l

Sodium depletion, renal loss (patient often hypovolaemic)

- diuretics
- Addison's
- diuretic stage of renal failure

Patient often euvolaemic

- SIADH (urine osmolality > 500 mmol/kg)
- hypothyroidism

### Urinary sodium < 20 mmol/l

Sodium depletion, extra-renal loss

- diarrhoea, vomiting, sweating
- burns, adenoma of rectum

Water excess (patient often hypervolaemic and oedematous)

- secondary hyperaldosteronism: CCF, cirrhosis
- reduced GFR: renal failure
- IV dextrose, psychogenic polydipsia

You are performing a study of blood pressure readings in patients with chronic kidney disease. Assuming that the results are normally distributed, what percentage of values lie within two standard deviations of the mean blood pressure reading?

<input type="radio"/>	A. 95.4%
<input type="radio"/>	B. 5.3%
<input type="radio"/>	C. 98.3%
<input type="radio"/>	D. 10%
<input type="radio"/>	E. 97.5%

[Next question](#)

### Normal distribution

The normal distribution is also known as the Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

#### Properties of the Normal distribution

- symmetrical i.e. Mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 \* SD) to the mean + (1.96 \* SD) is called the 95% confidence interval, i.e. If a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

#### Standard deviation

- the standard deviation (SD) is a measure of how much dispersion exists from the mean
- SD = square root (variance)



Doxazosin is a:

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Alpha-1 antagonist             |
| <input type="radio"/> | B. Alpha-1 agonist                |
| <input type="radio"/> | C. Non-selective alpha antagonist |
| <input type="radio"/> | D. Alpha-2 agonist                |
| <input type="radio"/> | E. Alpha-2 antagonist             |

Next question

Doxazosin is an alpha-1 adrenoceptor antagonist used in the treatment of hypertension and benign prostatic hypertrophy

### Adrenoceptor antagonists

Alpha antagonists

- alpha-1: doxazosin
- alpha-1a: tamsulosin - acts mainly on urogenital tract
- alpha-2: yohimbine
- non-selective: phenoxybenzamine (previously used in peripheral arterial disease)

Beta antagonists

- beta-1: atenolol
- non-selective: propranolol

Carvedilol and labetalol are mixed alpha and beta antagonists

A new oral-hypoglycaemic is being developed. A number of different study types are considered to demonstrate efficacy in reducing the HbA1c. Which one of the following study designs would require the most patients to produce a significant result?

<input type="radio"/>	A. Equivalence trial
<input type="radio"/>	B. Non-inferiority trial
<input type="radio"/>	C. Superiority trial
<input type="radio"/>	D. Placebo-controlled trial
<input type="radio"/>	E. Study design would not affect the number of patients required

[Next question](#)

As a superiority trial compares the new drug with an existing treatment, which would also lower HbA1c, a large sample size is required to demonstrate a significant difference.

### Study design: new drugs

When a new drug is launched there are a number of options available in terms of study design. One option is a placebo controlled trial. Whilst this may provide robust evidence it may be considered unethical if established treatments are available and it also does not provide a comparison with standard treatments.

If a drug is therefore to be compared to an existing treatment a statistician will need to decide whether the trial is intended to show superiority, equivalence or non-inferiority:

- superiority: whilst this may seem the natural aim of a trial one problem is the large sample size needed to show a significant benefit over an existing treatment
- equivalence: an equivalence margin is defined ( $-\delta$  to  $+\delta$ ) on a specified outcome. If the confidence interval of the difference between the two drugs lies within the equivalence margin then the drugs may be assumed to have a similar effect
- non-inferiority: similar to equivalence trials, but only the lower confidence interval needs to lie within the equivalence margin (i.e.  $-\delta$ ). Small sample sizes are needed for these trials. Once a drug has been shown to be non-inferior large studies may be performed to show superiority

It should be remembered that drug companies may not necessarily want to show superiority over an existing product. If it can be demonstrated that their product is equivalent or even non-inferior then they may compete on price or convenience.

Which one of the following statements regarding glucagon-like peptide-1 (GLP-1) is incorrect?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Secreted in response to an oral glucose load          |
| <input type="radio"/> | B. Increased levels are seen in type 2 diabetes mellitus |
| <input type="radio"/> | C. Slows gastric emptying                                |
| <input type="radio"/> | D. Secreted by the small intestine                       |
| <input type="radio"/> | E. Responsible for the incretin effect                   |

Next question

Decreased levels of GLP-1 are seen in type 2 diabetes mellitus

### Diabetes mellitus: GLP-1 and the new drugs

A number of new drugs to treat diabetes mellitus have become available in recent years. Much research has focused around the role of glucagon-like peptide-1 (GLP-1), a hormone released by the small intestine in response to an oral glucose load

Whilst it is well known that insulin resistance and insufficient B-cell compensation occur other effects are also seen in type 2 diabetes mellitus (T2DM). In normal physiology an oral glucose load results in a greater release of insulin than if the same load is given intravenously - this known as the incretin effect. This effect is largely mediated by GLP-1 and is known to be decreased in T2DM.

Increasing GLP-1 levels, either by the administration of an analogue or inhibiting its breakdown, is therefore the target of two recent classes of drug

Glucagon-like peptide-1 (GLP-1) mimetics (e.g. exenatide)

- increase insulin secretion and inhibit glucagon secretion
- licensed for use in T2DM
- must be given by subcutaneous injection within 60 minutes before the morning and evening meals. It should not be given after a meal
- may be combined with metformin, a sulfonylurea or a thiazolidinedione
- typically results in weight loss
- major adverse effect is nausea and vomiting

NICE guidelines on the use of exenatide

- should be used only when insulin would otherwise be started, obesity is a problem (BMI > 35 kg/m<sup>2</sup>) and the need for high dose insulin is likely
- continue only if beneficial response occurs and is maintained (> 1.0 percentage point HbA1c reduction and weight loss > 3% in 6 months)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings on the use of exenatide:

- increased risk of severe pancreatitis
- increased risk of renal impairment

Dipeptidyl peptidase-4 (DPP-4) inhibitors (e.g. Vildagliptin, sitagliptin)

- oral preparation
- trials to date show that the drugs are relatively well tolerated with no increased incidence of hypoglycaemia
- do not cause weight gain

NICE guidelines on DPP-4 inhibitors

- continue DPP-4 inhibitor only if there is a reduction of  $> 0.5$  percentage points in HBA1c in 6 months
- NICE suggest that a DPP-4 inhibitor might be preferable to a thiazolidinedione if further weight gain would cause significant problems, a thiazolidinedione is contraindicated or the person has had a poor response to a thiazolidinedione

A cohort study is being designed to look at the relationship between smoking and breast cancer. What is the usual outcome measure in a cohort study?

- ☐ A. Odds ratio
- ☐ B. Experimental event rate
- ☐ C. Relative risk
- ☐ D. Absolute risk increase
- ☐ E. Numbers needed to harm

[Next question](#)

Cohort studies - relative risk

## Study design

The following table highlights the main features of the main types of study:

<b>Randomised controlled trial</b>	<p>Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo)</p> <p>Practical or ethical problems may limit use</p>
<b>Cohort study</b>	<p>Observational and prospective. Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome.</p> <p>The usual outcome measure is the relative risk.</p> <p>Examples include Framingham Heart Study</p>
<b>Case-control study</b>	<p>Observational and retrospective. Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition.</p> <p>The usual outcome measure is the odds ratio.</p> <p>Inexpensive, produce quick results Useful for studying rare conditions Prone to confounding</p>
<b>Cross-sectional survey</b>	<p>Provide a 'snapshot', sometimes called prevalence studies</p> <p>Provide weak evidence of cause and effect</p>

Each one of the following may raise ESR, except:

<input type="radio"/>	A. Female sex
<input type="radio"/>	B. Systemic lupus erythematosus
<input type="radio"/>	C. Polycythaemia
<input type="radio"/>	D. Myeloma
<input type="radio"/>	E. Increasing age

Next question

### Erythrocyte sedimentation rate (ESR)

The ESR is a non-specific marker of inflammation and depends on both the size, shape and number of red blood cells and the concentration of plasma proteins such as fibrinogen, alpha2-globulins and gamma globulins

Causes of a high ESR

- temporal arteritis
- myeloma
- other connective tissue disorders e.g. systemic lupus erythematosus
- other malignancies
- infection
- other factors which raise ESR: increasing age, female sex, anaemia

Causes of a low ESR

- polycythaemia
- afibrinogenaemia/hypofibrinogenaemia

**Question 48 of 402**

Next

A 25-year-old woman presents for review. She has a history of depression and is currently prescribed citalopram. Despite returning from a recent holiday in Spain she complains of feeling tired all the time. On examination you notice a slightly raised red rash on the bridge of her nose and cheeks. Although she complains of having 'stiff joints' you can find no evidence of arthritis. You order some basic blood tests:

Hb	12.7 g/dl
Platelets	$130 \times 10^9/l$
WBC	$3.3 \times 10^9/l$

Na <sup>+</sup>	138 mmol/l
K <sup>+</sup>	4.0 mmol/l
Urea	3.4 mmol/l
Creatinine	77 $\mu$ mol/l

Free T4	12.2 pmol/l
TSH	1.25 mu/l
CRP	9 mg/l

What is the most likely diagnosis?

<input type="radio"/>	A. Systemic lupus erythematosus
<input type="radio"/>	B. Acne rosacea
<input type="radio"/>	C. Fibromyalgia
<input type="radio"/>	D. Lyme Disease
<input type="radio"/>	E. HIV seroconversion illness

Next question

The malar rash, arthralgia, lethargy and history of mental health points towards a diagnosis of SLE. Remember that the CRP (in contrast to the ESR) is typically normal in SLE.

**SLE: features**

Systemic lupus erythematosus (SLE) is a multisystem, autoimmune disorder. It typically presents in early adulthood and is more common in women and people of Afro-Caribbean origin.

General features

- fatigue
- fever
- mouth ulcers
- lymphadenopathy

## Skin

- malar (butterfly) rash: spares nasolabial folds
- discoid rash: scaly, erythematous, well demarcated rash in sun-exposed areas. Lesions may progress to become pigmented and hyperkeratotic before becoming atrophic
- photosensitivity
- Raynaud's phenomenon
- livedo reticularis
- non-scarring alopecia

## Musculoskeletal

- arthralgia
- non-erosive arthritis

## Respiratory

- pleurisy
- fibrosing alveolitis

## Renal

- proteinuria
- glomerulonephritis (diffuse proliferative glomerulonephritis is the most common type)

## Neuropsychiatric

- anxiety and depression
- psychosis
- seizures



You are speaking to a 24-year-old man who is known to have haemophilia A. He asks you what the chances are of his future children developing haemophilia. What is the correct answer?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Same as background population level |
| <input type="radio"/> | B. 25%                                 |
| <input type="radio"/> | C. 50%                                 |
| <input type="radio"/> | D. 50% if male, 0% if female           |
| <input type="radio"/> | E. 100%                                |

[Next question](#)

X-linked recessive conditions - there is no male-to-male transmission. Affected males can only have unaffected sons and carrier daughters.

You should of course also discuss with him that any daughters that he has will be carriers of the condition.

### X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters.

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier.

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen.

**Question 50 of 402**

Next

A patient is seen in clinic complaining of abdominal pain. Routine bloods show:

Na <sup>+</sup>	142 mmol/l
K <sup>+</sup>	4.0 mmol/l
Chloride	104 mmol/l
Bicarbonate	19 mmol/l
Urea	7.0 mmol/l
Creatinine	112 µmol/l

What is the anion gap?

- ☐ A. 4 mmol/L
- ☐ B. 14 mmol/L
- ☐ C. 20 mmol/L
- ☐ D. 21 mmol/L
- ☐ E. 23 mmol/L

Next question

The anion gap may be calculated by using (sodium + potassium) - (bicarbonate + chloride)

$$= (142 + 4.0) - (104 + 19) = 23 \text{ mmol/L}$$

**Anion gap**

The anion gap is calculated by:

(sodium + potassium) - (bicarbonate + chloride)

A normal anion gap is 8-14 mmol/L

It is useful to consider in patients with a metabolic acidosis:

Causes of a normal anion gap or hyperchloraemic metabolic acidosis

- gastrointestinal bicarbonate loss: diarrhoea, ureterosigmoidostomy, fistula
- renal tubular acidosis
- drugs: e.g. acetazolamide
- ammonium chloride injection
- Addison's disease

## Causes of a raised anion gap metabolic acidosis

- lactate: shock, hypoxia
- ketones: diabetic ketoacidosis, alcohol
- urate: renal failure
- acid poisoning: salicylates, methanol

In the Gell and Coombs classification of hypersensitivity reactions Grave's disease is an example of a:

- |                       |                      |
|-----------------------|----------------------|
| <input type="radio"/> | A. Type I reaction   |
| <input type="radio"/> | B. Type II reaction  |
| <input type="radio"/> | C. Type III reaction |
| <input type="radio"/> | D. Type IV reaction  |
| <input type="radio"/> | E. Type V reaction   |

Next question

## Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

Type I - Anaphylactic

- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

Type II - Cell bound

- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

Type III - Immune complex

- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

Type IV - Delayed hypersensitivity

- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity

- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

A 61-year-old woman is admitted to the Acute Medical Unit as she is generally unwell with muscle twitching. Blood pressure is recorded at 114/78 mmHg, pulse 84/min and she is afebrile. Blood tests reveal the following:

Calcium	1.94 mmol/l
Albumin	38 g/l

Which one of the following tests is most useful in elucidating the cause of her symptoms?

- ☐ A. Urea
- ☐ B. Vitamin D
- ☐ C. Phosphate
- ☒ D. Parathyroid hormone
- ☐ E. Magnesium

Next question

Parathyroid hormone is the single most useful test in determining the cause of hypocalcaemia

### Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

#### Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)

Acute pancreatitis may also cause hypocalcaemia. Contamination of blood samples with EDTA may also give falsely low calcium levels

#### Management

- acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

Which one of the following statements best describes a type II statistical error?

- ☐ A. The p value fails to reach statistical significance
- ☐ B. A study fails to reach an appropriate power
- ☐ C. The null hypothesis is rejected when it is true
- ☐ D. The null hypothesis is accepted when it is false
- ☐ E. The alternative hypothesis is rejected when it is false

Next question

### Significance tests

A null hypothesis ( $H_0$ ) states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct.

For example:

- 'there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not'

The alternative hypothesis ( $H_1$ ) is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

The **p value** is the probability of obtaining a result by chance at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. It is therefore equal to the chance of making a type I error (see below).

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist, a false positive. This is determined against a preset significance level (termed alpha). As the significance level is determined in advance the chance of making a type I error is not affected by sample size. It is however increased if the number of end-points are increased. For example if a study has 20 end-points it is likely one of these will be reached, just by chance.
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists, a false negative. The probability of making a type II error is termed beta. It is determined by both sample size and alpha

	Study accepts $H_0$	Study rejects $H_0$
--	---------------------	---------------------

<b>Reality <math>H_0</math></b>		Type 1 error (alpha)
<b>Reality <math>H_1</math></b>	Type 2 error (beta)	Power (1 - beta)

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false, i.e. the probability of detecting a statistically significant difference

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Which one of the following clotting factors is not affected by warfarin?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Factor II  |
| <input type="radio"/> | B. Factor VII |
| <input type="radio"/> | C. Factor XII |
| <input type="radio"/> | D. Factor IX  |
| <input type="radio"/> | E. Factor X   |

Next question

Warfarin - clotting factors affected mnemonic - 1972 (10, 9, 7, 2)

Factor XII is not affected by warfarin

### Warfarin

Warfarin is an oral anticoagulant which inhibits the reduction of vitamin K to its active hydroquinone form, which in turn acts as a cofactor in the formation of clotting factor II, VII, IX and X (mnemonic = 1972) and protein C .

#### Indications

- venous thromboembolism: target INR = 2.5, if recurrent 3.5
- atrial fibrillation, target INR = 2.5
- mechanical heart valves, target INR depends on the valve type and location. Mitral valves generally require a higher INR than aortic valves.

Patients on warfarin are monitored using the INR (international normalised ration), the ratio of the prothrombin time for the patient over the normal prothrombin time. Warfarin has a long half-life and achieving a stable INR may take several days. There a variety of loading regimes and computer software is now often used to alter the dose.

#### Factors that may potentiate warfarin

- liver disease
- P450 enzyme inhibitors, e.g.: amiodarone, ciprofloxacin
- cranberry juice
- drugs which displace warfarin from plasma albumin, e.g. NSAIDs
- inhibit platelet function: NSAIDs

#### Side-effects



- haemorrhage
- teratogenic, although can be used in breast-feeding mothers
- skin necrosis: when warfarin is first started biosynthesis of protein C is reduced. This results in a temporary procoagulant state after initially starting warfarin, normally avoided by concurrent heparin administration. Thrombosis may occur in venules leading to skin necrosis
- purple toes

Which one of the following is involved in the degradation of polypeptides?

- ☐ A. Peroxisome
- ☐ B. Endoplasmic reticulum
- ☐ C. Proteasome
- ☐ D. Ribosome
- ☐ E. Golgi apparatus

Next question

## Cell organelles

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	Main function
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Aerobic respiration. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide
Proteasome	Along with lysosome pathway involved in degradation of large protein molecules

**Question 56 of 402**

Next

A 37-year-old man with a history of alcohol excess is admitted with alcohol-withdrawal seizures to the acute medical unit. Admission bloods show the following:

Na <sup>+</sup>	137 mmol/l
K <sup>+</sup>	3.0 mmol/l
Urea	2.0 mmol/l
Creatinine	78 µmol/l
Calcium	2.03 mmol/l

What other blood abnormality is he also most likely to have?

- ☐ A. Hypomagnesaemia
- ☐ B. Elevated ammonia levels
- ☐ C. Hypophosphataemia
- ☐ D. Partially compensated metabolic alkalosis
- ☐ E. Raised bilirubin

Next question

**Hypomagnesaemia**

Cause of low magnesium

- diuretics
- total parenteral nutrition
- diarrhoea
- alcohol
- hypokalaemia, hypocalcaemia

Features

- paraesthesia
- tetany
- seizures
- arrhythmias
- decreased PTH secretion --> hypocalcaemia
- ECG features similar to those of hypokalaemia
- exacerbates digoxin toxicity

A study is designed to assess a new proton pump inhibitor (PPI) in elderly patients who are taking aspirin. The new PPI is given to 120 patients whilst a control group of 240 is given the standard PPI. Over a five year period 24 of the group receiving the new PPI had an upper GI bleed compared to 60 who received the standard PPI. What is the absolute risk reduction?

- ☐ A. 15%
- ☐ B. 10%
- ☐ C. 12
- ☒ D. 5%
- ☐ E. 20

[Next question](#)

Absolute risk reduction = (Experimental event rate) - (Control event rate)

Control event rate =  $60 / 240 = 0.25$

Experimental event rate =  $24 / 120 = 0.2$

Absolute risk reduction =  $0.25 - 0.2 = 0.05 = 5\%$  reduction

### Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by  $1/(\text{Absolute risk reduction})$  and is rounded to the next highest whole number

Experimental event rate (EER) = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate (CER) = (Number who had particular outcome with the control/ (Total number who had the control)

### Absolute risk reduction = CER-EER or EER-CER?

The absolute risk reduction (ARR) may be calculated by finding the absolute difference between the control event rate (CER) and the experimental event rate (EER). You will often find both versions of the above listed in different sources. In some ways it doesn't matter which you use as you will end up with the same answer but from a technical point of view:

- if the outcome of the study is undesirable then  $ARR = CER - EER$
- if the outcome of the study is desirable then  $ARR^* = EER - CER$

\*this may be more accurately termed absolute benefit increase, rather than absolute risk reduction

Which one of the following statements regarding the power of a study is correct?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Is the probability of rejecting the null hypothesis when it is false |
| <input type="radio"/> | B. Decreases with increasing sample size                                |
| <input type="radio"/> | C. Lies within 2 standard deviations of the mean                        |
| <input type="radio"/> | D. Is the chance a significant p value will be reached                  |
| <input type="radio"/> | E. Is equal to 1 - (the probability of a type I error)                  |

Next question

Power = 1 - the probability of a type II error

### Significance tests

A null hypothesis ( $H_0$ ) states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct.

For example:

- 'there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not'

The alternative hypothesis ( $H_1$ ) is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

The **p value** is the probability of obtaining a result by chance at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. It is therefore equal to the chance of making a type I error (see below).

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist, a false positive. This is determined against a preset significance level (termed alpha). As the significance level is determined in advance the chance of making a type I error is not affected by sample size. It is however increased if the number of end-points are increased. For example if a study has 20 end-points it is likely one of these will be reached, just by chance.
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists, a false negative. The probability of making a type II error is termed beta. It is determined by both sample size and alpha

	Study accepts $H_0$	Study rejects $H_0$
Reality $H_0$		Type 1 error (alpha)
Reality $H_1$	Type 2 error (beta)	Power (1 - beta)

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false, i.e. the probability of detecting a statistically significant difference

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Immunoglobulin therapy may be indicated in each of the following except:

<input type="radio"/>	A. Dermatomyositis
<input type="radio"/>	B. Guillain-Barre syndrome
<input type="radio"/>	C. Kawasaki disease
<input type="radio"/>	D. Idiopathic thrombocytopenic purpura
<input type="radio"/>	E. Thrombotic thrombocytopenic purpura

Next question

The management of management thrombotic thrombocytopenic purpura involves steroids and immunosuppressants. Plasma exchange is also commonly used

### Immunoglobulins: therapeutics

The Department of Health issued guidelines on the use of intravenous immunoglobulins in May 2008

#### Uses

- primary and secondary immunodeficiency
- idiopathic thrombocytopenic purpura
- myasthenia gravis
- Guillain-Barre syndrome
- Kawasaki disease
- toxic epidermal necrolysis
- pneumonitis induced by CMV following transplantation
- low serum IgG levels following haematopoietic stem cell transplant for malignancy
- dermatomyositis
- chronic inflammatory demyelinating polyradiculopathy

#### Basics

- formed from large pool of donors (e.g. 5,000)
- IgG molecules with a subclass distribution similar to that of normal blood
- half-life of 3 weeks

A 64-year-old woman who is reviewed due to multiple non-healing leg ulcers. She reports feeling generally unwell for many months. Examination findings include a blood pressure of 138/72 mmHg, pulse 90 bpm, pale conjunctivae and poor dentition associated with bleeding gums. What is the most likely underlying diagnosis?

<input type="radio"/>	A. Thyrotoxicosis
<input type="radio"/>	B. Vitamin B12 deficiency
<input type="radio"/>	C. Vitamin C deficiency
<input type="radio"/>	D. Diabetes mellitus
<input type="radio"/>	E. Sarcoidosis

[Next question](#)

### Vitamin C deficiency

Vitamin C deficiency (scurvy) leads to defective synthesis of collagen resulting in capillary fragility (bleeding tendency) and poor wound healing

#### Features

- gingivitis, loose teeth
- poor wound healing
- bleeding from gums, haematuria, epistaxis
- general malaise



Which one of the following best describes the characteristics of a negatively skewed distribution?

- |                       |                         |
|-----------------------|-------------------------|
| <input type="radio"/> | A. Median < mode < mean |
| <input type="radio"/> | B. Mean < median < mode |
| <input type="radio"/> | C. Mode < mean < median |
| <input type="radio"/> | D. Median < mean < mode |
| <input type="radio"/> | E. Mean < mode < median |

Next question

#### Skewed distributions

- alphabetical order: mean - median - mode
- '>' for positive, '<' for negative

#### Skewed distributions

Normal distributions: mean = median = mode

Positively skewed distribution: mean > median > mode

Negatively skewed distribution mean < median < mode

To remember the above note how they are in alphabetical order, think positive going forward with '>', whilst negative going backwards '<'

A 14-year-old girl is admitted to the Emergency Department. Over the past hour she has developed a painless, non-pruritic erythematous rash associated with severe angioedema. She has a past medical history of recurrent abdominal pain. Her symptoms fail to respond to adrenaline and she is therefore intubated to protect the airway. She is discharged from ITU after three days. During outpatient follow-up two weeks later a diagnosis of hereditary angioedema is suspected. What is the most appropriate screening test to perform?

- |                                  |                          |
|----------------------------------|--------------------------|
| <input type="radio"/>            | A. Serum IgE levels      |
| <input type="radio"/>            | B. Serum C3 levels       |
| <input type="radio"/>            | C. Serum tryptase levels |
| <input checked="" type="radio"/> | D. Serum C4 levels       |
| <input type="radio"/>            | E. Serum C1-INH levels   |

[Next question](#)

Hereditary angioedema - C4 is the best screening test inbetween attacks

## Hereditary angioedema

Hereditary angioedema is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

### Investigation

- C1-INH level is low during an attack
- low C2 and C4 levels are seen, even between attacks. Serum C4 is the most reliable and widely used screening tool

### Symptoms

- attacks may be preceded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

### Management

- acute: IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help

Which one of the following adrenoceptors cause vasoconstriction and relaxation of GI muscle in response to sympathetic stimulation?

<input type="radio"/>	A. Alpha-1
<input type="radio"/>	B. Alpha-2
<input type="radio"/>	C. Beta-1
<input type="radio"/>	D. Beta-2
<input type="radio"/>	E. Beta-3

[Next question](#)

### Adrenoceptors

#### Alpha-1

- vasoconstriction
- relaxation of GI smooth muscle
- salivary secretion
- hepatic glycogenolysis

#### Alpha-2

- mainly presynaptic: inhibition of transmitter release (inc NA, Ach from autonomic nerves)
- inhibits insulin
- platelet aggregation

#### Beta-1

- mainly located in the heart
- increase heart rate + force

#### Beta-2

- vasodilation
- bronchodilation
- relaxation of GI smooth muscle

#### Beta-3

- lipolysis

## Pathways

- all are G-protein coupled
- alpha-1: activate phospholipase C --> IP3 --> DAG
- alpha-2: inhibit adenylate cyclase
- beta-1: stimulate adenylate cyclase
- beta-2: stimulate adenylate cyclase
- beta-3: stimulate adenylate cyclase

**Question 64 of 402**

Next

A 66-year-old comes for review. He had a prosthetic aortic valve replacement five years ago for which he is warfarinised. Over the past three months he has been complaining of fatigue and a full blood count was requested:

Hb	10.3 g/dl
MCV	68 fl
Plt	$356 \times 10^9/l$
WBC	$5.2 \times 10^9/l$
Blood film	Hypochromia
INR	3.0

An upper GI endoscopy was reported as normal. What is the most appropriate next investigation?

- ☐ A. Transthoracic echocardiogram
- ☐ B. Colonoscopy
- ☐ C. Three sets of blood cultures
- ☐ D. Transoesophageal echocardiogram
- ☐ E. Reticulocyte count

Next question

Any patient of this age with an unexplained microcytic anaemia should have a lower gastrointestinal tract investigation to exclude colorectal cancer

**Colorectal cancer: referral guidelines**

NICE recommend the following patients are referred urgently (i.e. within 2 weeks) to colorectal services for investigation:

- patients > 40 years old, reporting rectal bleeding with a change of bowel habit towards looser stools and/or increased stool frequency persisting for 6 weeks or more
- patients > 60 years old, with rectal bleeding persisting for 6 weeks or more without a change in bowel habit and without anal symptoms
- patients > 60 years old, with a change in bowel habit to looser stools and/or more frequent stools persisting for 6 weeks or more without rectal bleeding
- any patient presenting with a right lower abdominal mass consistent with involvement of the large bowel
- any patient with a palpable rectal mass
- unexplained iron deficiency anaemia in men or non-menstruating women (Hb < 11 g/dl in men, < 10 g/dl in women)

What is the mode of inheritance of vitamin D-resistant rickets?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. X-linked dominant         |
| <input type="radio"/> | B. Autosomal recessive       |
| <input type="radio"/> | C. Autosomal dominant        |
| <input type="radio"/> | D. Mitochondrial inheritance |
| <input type="radio"/> | E. X-linked recessive        |

Next question

### Vitamin D-resistant rickets

Vitamin D-resistant rickets is a X-linked dominant condition which usually presents in infancy with failure to thrive. It is caused by impaired phosphate reabsorption in the renal tubules

#### Features

- failure to thrive
- normal serum calcium, low phosphate, elevated alkaline phosphatase
- x-ray changes: cupped metaphyses with widening of the epiphyses

Diagnosis is made by demonstrating increased urinary phosphate

#### Management

- high-dose vitamin D supplements
- oral phosphate supplements

A 43-year-old man has a routine medical for insurance purposes. The following result is obtained:

Uric acid	622 $\mu\text{mol/l}$ (210 - 480)
-----------	-----------------------------------

He is well with no significant past medical history. What is the most appropriate test to perform next?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Lipid profile         |
| <input type="radio"/> | B. Thyroid function test |
| <input type="radio"/> | C. Calcium               |
| <input type="radio"/> | D. Parathyroid hormone   |
| <input type="radio"/> | E. Pyrophosphate levels  |

Next question

Hyperuricaemia may be associated with both hyperlipidaemia and hypertension. It may also be seen in conjunction with the metabolic syndrome

### Hyperuricaemia

Increased levels of uric acid may be seen secondary to either increased cell turnover or reduced renal excretion of uric acid. Hyperuricaemia may be found in asymptomatic patients who have not experienced attacks of gout

Hyperuricaemia may be associated with hyperlipidaemia and hypertension. It may also be seen in conjunction with the metabolic syndrome

Increased synthesis

- Lesch-Nyhan disease
- myeloproliferative disorders
- diet rich in purines
- exercise
- psoriasis
- cytotoxics

Decreased excretion

- drugs: low-dose aspirin, diuretics, pyrazinamide
- pre-eclampsia
- alcohol
- renal failure
- lead

**Question 67 of 402**

Next

A 27-year-old man is reviewed in a fertility clinic. Semen analysis has revealed azoospermia. On examination at the previous appointment he was noted to be 1.83 metres tall with a body mass index of 25 kg / m<sup>2</sup>. A degree of gynaecomastia is noted, testicular volume is around 10ml bilaterally and his visual fields were normal. Which investigation is likely to be diagnostic?

- |                       |                         |
|-----------------------|-------------------------|
| <input type="radio"/> | A. FISH analysis of DNA |
| <input type="radio"/> | B. Prolactin level      |
| <input type="radio"/> | C. Karyotype            |
| <input type="radio"/> | D. MRI pituitary        |
| <input type="radio"/> | E. PCR analysis of DNA  |

Next question

Klinefelter's? - do a karyotype

**Klinefelter's syndrome**

Klinefelter's syndrome is associated with karyotype 47, XXY

**Features**

- often taller than average
- lack of secondary sexual characteristics
- small, firm testes
- infertile
- gynaecomastia - increased incidence of breast cancer
- elevated gonadotrophin levels

Diagnosis is by chromosomal analysis



A 65-year-old woman is investigated for a 6 week history of worsening shortness of breath, lethargy and weight loss. Her past medical history includes chronic obstructive pulmonary disease, hypertension and she is an ex-smoker. Clinical examination is unremarkable. Investigation results are as follows:

#### Chest x-ray

Hyperinflated lung fields, normal heart size

#### Bloods

Sodium	131 mmol/l
Potassium	3.4 mmol/l
Urea	7.2 mmol/l
Creatinine	101 $\mu$ mol/l
Hb	10.4 g/dl
MCV	91 fl
Plt	$452 \times 10^9/l$
WBC	$3.7 \times 10^9/l$

What is the most appropriate management?

- ☐ A. Screen for depression
- ☐ B. Short synacthen test
- ☐ C. Urgent referral to the chest clinic
- ☐ D. Stop bendroflumethiazide
- ☐ E. Urgent gastroscopy

Next question

Despite a normal chest x-ray an ex-smoker with shortness of breath, weight loss and hyponatraemia should be investigated on an urgent basis for lung cancer. This approach is supported by current NICE guidelines. Whilst gastrointestinal cancer is a possibility the normal MCV is not entirely consistent with chronic blood loss

#### Lung cancer: referral

The 2005 NICE cancer referral guidelines gave the following advice:

Consider immediate referral for patients with:

- signs of superior vena caval obstruction (swelling of the face/neck with fixed elevation of jugular venous pressure)

- stridor

Refer urgently patients with:

- persistent haemoptysis (in smokers or ex-smokers aged 40 years and older)
- a chest X-ray suggestive of lung cancer (including pleural effusion and slowly resolving consolidation)
- a normal chest X-ray where there is a high suspicion of lung cancer
- a history of asbestos exposure and recent onset of chest pain, shortness of breath or unexplained systemic symptoms where a chest x-ray indicates pleural effusion, pleural mass or any suspicious lung pathology

Refer urgently for chest x-ray for patients with any of the following:

- haemoptysis
- unexplained or persistent (longer than 3 weeks): chest and/or shoulder pain, dyspnoea, weight loss, chest signs, hoarseness, finger clubbing, cervical or supraclavicular lymphadenopathy, cough, features suggestive of metastasis from a

lung cancer (for example, secondaries in the brain, bone, liver, skin)

- underlying chronic respiratory problems with unexplained changes in existing symptoms

Which one of the following molecules acts as the co-receptor for cells expressing antigens combined with HLA class I molecules?

- ☐ A. CD4
- ☐ B. CD2b
- ☐ C. CD1
- ☒ D. CD8
- ☐ E. CD2

[Next question](#)

### Clusters of differentiation

The table below lists the major clusters of differentiation (CD) molecules

CD1	HLA molecule that presents lipid molecules
CD2	Found on thymocytes, T cells, and some natural killer cells that acts as a ligand for CD58 and CD59 and is involved in signal transduction and cell adhesion
CD3	The signalling component of the T cell receptor (TCR) complex
CD4	Co-receptor for HLA class II; also a receptor used by HIV to enter T cells
CD8	Co-receptor for HLA class I; also found on a subset of myeloid dendritic cells

**Question 70 of 402**

Next

You are asked to review some arterial blood gases (ABGs) done on a patient who has recently been admitted to the Emergency Department. The ABGs shown below were taken on air:

pH	7.53
pCO <sub>2</sub>	5.1 kPa
pO <sub>2</sub>	13.9 kPa

Which one of the following is the most likely cause?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Chronic obstructive pulmonary disease |
| <input type="radio"/> | B. Renal tubular acidosis                |
| <input type="radio"/> | C. Mesenteric ischaemia                  |
| <input type="radio"/> | D. Anxiety                               |
| <input type="radio"/> | E. Vomiting                              |

The blood gases show a metabolic alkalosis

**Metabolic alkalosis**

Metabolic alkalosis may be caused by a loss of hydrogen ions or a gain of bicarbonate. It is due mainly to problems of the kidney or gastrointestinal tract

**Causes**

- vomiting / aspiration (e.g. peptic ulcer leading to pyloric stenosis, nasogastric suction)
- diuretics
- liquorice, carbenoxolone
- hypokalaemia
- primary hyperaldosteronism
- Cushing's syndrome
- Bartter's syndrome
- congenital adrenal hyperplasia

**Mechanism of metabolic alkalosis**

- activation of renin-angiotensin II-aldosterone (RAA) system is a key factor
- aldosterone causes reabsorption of Na<sup>+</sup> in exchange for H<sup>+</sup> in the distal convoluted tubule
- ECF depletion (vomiting, diuretics) --> Na<sup>+</sup> and Cl<sup>-</sup> loss --> activation of RAA system --> raised aldosterone levels
- in hypokalaemia, K<sup>+</sup> shift from cells --> ECF, alkalosis is caused by shift of H<sup>+</sup> into cells to maintain neutrality

Which one of the following is the best definition of the p value?

- |                       |    |   |
|-----------------------|----|---|
| <input type="radio"/> | A. | The probability of obtaining a similar result, assuming that the null hypothesis is true              |
| <input type="radio"/> | B. | The probability that a replicating experiment would not yield the same conclusion                     |
| <input type="radio"/> | C. | The probability of obtaining a result at least as extreme, assuming that the null hypothesis is true  |
| <input type="radio"/> | D. | The probability that the null hypothesis is true  |
| <input type="radio"/> | E. | The probability of obtaining a result at least as extreme, assuming that the null hypothesis is false |

Next question

### Significance tests

A null hypothesis ( $H_0$ ) states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct.

For example:

- 'there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not'

The alternative hypothesis ( $H_1$ ) is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

The **p value** is the probability of obtaining a result by chance at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. It is therefore equal to the chance of making a type I error (see below).

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist, a false positive. This is determined against a preset significance level (termed alpha). As the significance level is determined in advance the chance of making a type I error is not affected by sample size. It is however increased if the number of end-points are increased. For example if a study has 20 end-points it is likely one of these will be reached, just by chance.
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists, a false negative. The probability of making a type II error is termed beta. It is determined by both sample size and alpha

	Study accepts $H_0$	Study rejects $H_0$
Reality $H_0$		Type 1 error (alpha)
Reality $H_1$	Type 2 error (beta)	Power (1 - beta)

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false, i.e. the probability of detecting a statistically significant difference

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Which of the following conditions is inherited in an autosomal dominant fashion?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Noonan syndrome                |
| <input type="radio"/> | B. Homocystinuria                 |
| <input type="radio"/> | C. Cystinuria                     |
| <input type="radio"/> | D. Congenital adrenal hyperplasia |
| <input type="radio"/> | E. Fanconi anaemia                |

Next question

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

### Autosomal dominant conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal dominant:

- Achondroplasia
- Acute intermittent porphyria
- Adult polycystic disease
- Antithrombin III deficiency
- Ehlers-Danlos syndrome
- Familial adenomatous polyposis
- Hereditary haemorrhagic telangiectasia
- Hereditary spherocytosis
- Hereditary non-polyposis colorectal carcinoma
- Huntington's disease
- Hyperlipidaemia type II
- Hypokalaemic periodic paralysis
- Malignant hyperthermia
- Marfan's syndromes

- Myotonic dystrophy
- Neurofibromatosis
- Noonan syndrome
- Osteogenesis imperfecta
- Peutz-Jeghers syndrome
- Retinoblastoma
- Romano-Ward syndrome
- Tuberose sclerosis
- Von Hippel-Lindau syndrome
- Von Willebrand's disease\*

\*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease



A 14-year-old girl presents with a swollen left knee. Her parents state she suffers from haemophilia and has been treated for a right-sided haemarthrosis previously. What other condition is she most likely to have?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Turner's syndrome     |
| <input type="radio"/> | B. Down's syndrome       |
| <input type="radio"/> | C. Ataxia telangiectasia |
| <input type="radio"/> | D. Hunter's syndrome     |
| <input type="radio"/> | E. Coeliac disease       |

[Next question](#)

Haemophilia is a X-linked recessive disorder and would hence be expected only to occur in males. As patients with Turner's syndrome only have one X chromosome however, they may develop X-linked recessive conditions

### X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters.

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier.

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen.

Which one of the following statements regarding interleukin 1 (IL-1) is true?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. It is released mainly by macrophages/monocytes                       |
| <input type="radio"/> | B. It causes vasoconstriction   |
| <input type="radio"/> | C. It reduces expression of selectin molecules on the endothelium       |
| <input type="radio"/> | D. IL-1 antagonists are currently licensed for use in colorectal cancer |
| <input type="radio"/> | E. It inhibits the release of nitric oxide by the endothelium           |

Next question

## IL-1

Interleukin 1 (IL-1) is a key mediator of the immune response. It is secreted mainly by macrophages and monocytes and acts as a costimulator of T cell and B cell proliferation.

Other effects include increasing the expression of adhesion molecules on the endothelium. By stimulating the release by the endothelium of vasoactive factors such as PAF, nitric oxide and prostacyclin it also causes vasodilation and increases vascular permeability. It is therefore one of the mediators of shock in sepsis. Along with IL-6 and TNF, it acts on the hypothalamus causing pyrexia.

**Question 75 of 402**[Next](#)

A study looks at the chance of having a myocardial infarction (MI) in patients with known ischaemic heart disease. Group A are given standard treatment. After 5 years 20 of the 100 patients have had a MI. Group B have standard treatment plus a new cardiac drug. After 5 years 10 of the 60 patients have had an MI. What is the odds ratio of having a MI whilst taking the new drug compared to those who do not?

- ☐ A. 0.8
- ☐ B. 0.83
- ☐ C. 2
- ☐ D. 1.2
- ☐ E. 1.25

[Next question](#)

Odds - remember a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome

NOT a ratio of the number of people who incur a particular outcome to the total number of people

Odds of MI in group B =  $10/50 = 1/5$

Odds of MI in group A =  $20/80 = 1/4$

Odds ratio of having a MI =  $1/5$  divided by  $1/4 = 0.8$

**Odds and odds ratio**

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome. The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control.

Odds ratios are the usual reported measure in case-control studies. It approximates to relative risk if the outcome of interest is rare.

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Achieved = 50% pain relief
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol =  $40 / 20 = 2$

The odds of achieving significant pain relief with placebo =  $30 / 60 = 0.5$

Therefore the odds ratio =  $2 / 0.5 = 4$

Which one of the following is not associated with hypocalcaemia combined with a raised phosphate level?

<input type="radio"/>	A. Chronic renal failure
<input type="radio"/>	B. Pseudohypoparathyroidism
<input type="radio"/>	C. Hypoparathyroidism
<input type="radio"/>	D. Osteomalacia
<input type="radio"/>	E. Acute rhabdomyolysis

Next question

Osteomalacia causes hypocalcaemia associated with a low serum phosphate, rather than a raised phosphate level.

### Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

#### Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)

Acute pancreatitis may also cause hypocalcaemia. Contamination of blood samples with EDTA may also give falsely low calcium levels

#### Management

- acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

A 40-year-old man presents with pain in his lower back and 'sciatica' for the past three days. He describes bending down to pick up a washing machine when he felt 'something go'. He now has severe pain radiating from his back down the right leg. On examination he describes paraesthesia over the anterior aspect of the right knee and the medial aspect of his calf. Power is intact and the right knee reflex is diminished. The femoral stretch test is positive on the right side. Which nerve root is most likely to be affected?

- ☐ A. Common peroneal nerve
- ☐ B. Lateral cutaneous nerve of the thigh
- ☐ C. L5
- ☐ D. L3
- ☐ E. L4

[Next question](#)

### Lower back pain: prolapsed disc

A prolapsed lumbar disc usually produces clear dermatomal leg pain associated with neurological deficits.

#### Features

- leg pain usually worse than back
- pain often worse when sitting

The table below demonstrates the expected features according to the level of compression:

<b>L3 nerve root compression</b>	Sensory loss over anterior thigh Weak quadriceps Reduced knee reflex Positive femoral stretch test
<b>L4 nerve root compression</b>	Sensory loss anterior aspect of knee Weak quadriceps Reduced knee reflex Positive femoral stretch test
<b>L5 nerve root compression</b>	Sensory loss dorsum of foot Weakness in foot and big toe dorsiflexion Reflexes intact Positive sciatic nerve stretch test
<b>S1 nerve root compression</b>	Sensory loss posterolateral aspect of leg and lateral aspect of foot Weakness in plantar flexion of foot Reduced ankle reflex Positive sciatic nerve stretch test

#### Management

- similar to that of other musculoskeletal lower back pain: analgesia, physiotherapy, exercises
- if symptoms persist then referral for consideration of MRI is appropriate

The muscarinic acetylcholine receptor is an example of a:

<input type="radio"/>	A. Ligand-gated ion channel
<input type="radio"/>	B. Tyrosine kinase receptor
<input type="radio"/>	C. Guanylate cyclase receptor
<input type="radio"/>	D. G protein-coupled receptor
<input type="radio"/>	E. Intracellular receptor

Next question

## Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

Ligand-gated ion channel

- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

Tyrosine kinase receptors

- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors

- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors

- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

**Question 79 of 402**

Next

An endocrinologist performs a study to assess whether a patient's HbA1c level is correlated to their LDL level. Assuming both HbA1c and LDL are normally distributed, which one of the following statistical tests is it most appropriate to perform?

<input type="radio"/>	A. Chi-squared test
<input type="radio"/>	B. Pearson's product-moment coefficient
<input type="radio"/>	C. Mann-Whitney test
<input type="radio"/>	D. Spearman's rank correlation coefficient
<input type="radio"/>	E. McNemar's test

Next question

**Correlation**

- parametric (normally distributed): Pearson's coefficient
- non-parametric: Spearman's coefficient

Pearson's product-moment coefficient test is most appropriate as the data is parametric and the study is assessing the correlation of two variables

McNemar's test is a non-parametric method used on nominal data to determine whether the row and column marginal frequencies are equal

**Significance tests: types**

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

**Parametric tests**

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

**Non-parametric tests**

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation



Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

During which of the following stages of mitosis does chromatin condense to form chromosomes?

<input type="radio"/>	A. Telophase
<input type="radio"/>	B. Metaphase
<input type="radio"/>	C. Prophase
<input type="radio"/>	D. Interphase
<input type="radio"/>	E. Anaphase

[Next question](#)

## Cell division

There are two types of cell division; mitosis and meiosis.

Mitosis	Meiosis
Occurs in somatic cells	Occurs in gametes
Results in 2 diploid daughter cells	Results in 4 haploid daughter cells
Daughter cells are genetically identical to parent cell	Daughter cells contain one homologue of each chromosome pair and are therefore genetically different

Remember:

- somatic cells have 22 pairs of autosomes and 1 pair of sex chromosomes, i.e. 46XY or 46XX
- cells with a normal chromosome complement are known as diploid cells
- gametes (ova or spermatozoa) have a single copy of each chromosome and are known as haploid cells

## Mitosis

Mitosis occurs during the M phase of the cell cycle. It describes the process in which somatic cells divide and replicate producing genetically identical diploid daughter cells. This allows tissue to grow and renew itself.

During the S phase of the cell cycle the cell prepares itself for division by duplicating the chromosomes. The table below shows the phases of mitosis itself:

<b>Prophase</b>	Chromatin in the nucleus condenses
<b>Prometaphase</b>	Nuclear membrane breaks down allowing the microtubules to attach to the chromosomes
<b>Metaphase</b>	Chromosomes aligned at middle of cell
<b>Anaphase</b>	The paired chromosomes separate at the kinetochores and move to opposite sides of the cell
<b>Telophase</b>	Chromatids arrive at opposite poles of cell
<b>Cytokinesis</b>	Actin-myosin complex in the centre of the cell contracts resulting in it being 'pinched' into two daughter cells

Which one of the following karyotypes is associated with short stature?

<input type="radio"/>	A. 45,XO
<input type="radio"/>	B. 46,YO
<input type="radio"/>	C. 46,XO
<input type="radio"/>	D. 47,XYY
<input type="radio"/>	E. 47,XXY

Next question

### Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

#### Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

T-Helper cells of the Th2 subset typically secrete:

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. IL-4, IL-5, IL-6, IL-10, IL-13 |
| <input type="radio"/> | B. IFN-gamma, IL-2, IL-3          |
| <input type="radio"/> | C. IL-1, IL-6, TNF-alpha          |
| <input type="radio"/> | D. IFN-beta, IL-4, IL-8           |
| <input type="radio"/> | E. IL-1                           |

Next question

### T-Helper cells

There are two major subsets of T-Helper cells:

Th1

- involved in the cell mediated response and delayed (type IV) hypersensitivity
- secrete IFN-gamma, IL-2, IL-3

Th2

- involved in mediating humoral (antibody) immunity
- e.g. stimulating production of IgE in asthma
- secrete IL-4, IL-5, IL-6, IL-10, IL-13

A patient with lung cancer has a Positron Emission Tomography (PET) scan to evaluate possible metastatic disease. What does this type of scan demonstrate?

<input type="radio"/>	A. Cellular proliferation
<input type="radio"/>	B. Apoptotic activity
<input type="radio"/>	C. Glucose uptake
<input type="radio"/>	D. Vascular supply
<input type="radio"/>	E. Tyrosine kinase activity

[Next question](#)

### Positron Emission Tomography (PET)

Positron Emission Tomography (PET) is a form of nuclear imaging which uses fluorodeoxyglucose (FDG) as the radiotracer. This allows a 3D image of metabolic activity to be generated using glucose uptake as a proxy marker. The images obtained are then combined with a conventional imaging technique such as CT to decide whether lesions are metabolically active.

#### Uses

- evaluating primary and possible metastatic disease
- cardiac PET: not used mainstream currently

How is the left ventricular ejection fraction calculated?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. End systolic LV volume / end diastolic LV volume |
| <input type="radio"/> | B. End diastolic LV volume / end systolic LV volume |
| <input type="radio"/> | C. End diastolic LV volume / stroke volume          |
| <input type="radio"/> | D. End systolic LV volume - end diastolic LV volume |
| <input type="radio"/> | E. Stroke volume / end diastolic LV volume          |

Next question

## Cardiovascular physiology

### Left ventricular ejection fraction

Left ventricular ejection fraction = (stroke volume / end diastolic LV volume ) \* 100%

Stroke volume = end diastolic LV volume - end systolic LV volume

### Pulse pressure

Pulse pressure = Systolic Pressure - Diastolic Pressure

Factors which increase pulse pressure

- a less compliant aorta (this tends to occur with advancing age)
- increased stroke volume

Which one of the following is associated with increased lung compliance?

<input type="radio"/>	A. Kyphosis
<input type="radio"/>	B. Pulmonary oedema
<input type="radio"/>	C. Emphysema
<input type="radio"/>	D. Pulmonary fibrosis
<input type="radio"/>	E. Pneumonectomy

Next question

### Respiratory physiology: lung compliance

Lung compliance is defined as change in lung volume per unit change in airway pressure

Causes of increased compliance

- age
- emphysema - this is due to loss alveolar walls and associated elastic tissue

Causes of decreased compliance

- pulmonary oedema
- pulmonary fibrosis
- pneumonectomy
- kyphosis

Which cell organelle is involved in the breakdown of oligopeptides?

- ☐ A. Golgi apparatus
- ☐ B. Rough endoplasmic reticulum
- ☐ C. Peroxisome
- ☐ D. Lysosome
- ☐ E. Smooth endoplasmic reticulum

[Next question](#)

Protein degradation in eukaryotes is also carried out by protein complexes called proteasomes.

### Cell organelles

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	Main function
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Aerobic respiration. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide
Proteasome	Along with lysosome pathway involved in degradation of large protein molecules



Where is CCK secreted from?

- ☐ A. I cells in upper small intestine
- ☐ B. G cells in stomach
- ☐ C. K cells in upper small intestine
- ☐ D. D cells in the pancreas
- ☐ E. S cells in upper small intestine

[Next question](#)

### Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
<b>Gastrin</b>	G cells in antrum of the stomach	Distension of stomach, vagus nerves (mediated by gastrin-releasing peptide), luminal peptides/amino acids Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
<b>CCK</b>	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
<b>Secretin</b>	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
<b>VIP</b>	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid secretion
<b>Somatostatin</b>	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production

Aldosterone is secreted by the:

<input type="radio"/>	A. Juxtaglomerular apparatus
<input type="radio"/>	B. Zona glomerulosa
<input type="radio"/>	C. Posterior pituitary
<input type="radio"/>	D. Zona reticularis
<input type="radio"/>	E. Zona fasciculata

Next question

Adrenal cortex mnemonic: GFR - ACD

### Renin-angiotensin-aldosterone system

Adrenal cortex (mnemonic **GFR - ACD**)

- zona **g**lomerulosa (on outside): mineralocorticoids, mainly **a**ldosterone
- zona **f**asciculata (middle): glucocorticoids, mainly **c**ortisol
- zona **r**eticularis (on inside): androgens, mainly **d**ehydroepiandrosterone (DHEA)

Renin

- released by juxtaglomerular apparatus (JGA) cells in kidney in response to reduced renal perfusion, low sodium
- hydrolyses angiotensinogen to form angiotensin I

Factors stimulating renin secretion

- low BP
- hyponatraemia
- sympathetic nerve stimulation
- catecholamines
- erect posture

Angiotensin

- ACE in lung converts angiotensin I --> angiotensin II

- causes vasoconstriction of vascular smooth muscle leading to raised BP and vasoconstriction of efferent arteriole of the glomerulus
- stimulates thirst
- stimulates aldosterone and ADH release

#### Aldosterone

- released by the zona glomerulosa in response to raised angiotensin II, potassium, and ACTH levels
- causes retention of  $\text{Na}^+$  in exchange for  $\text{K}^+/\text{H}^+$  in distal tubule

Where are G protein-coupled receptors located?

<input type="radio"/>	A. Nucleus
<input type="radio"/>	B. Golgi apparatus
<input type="radio"/>	C. Ribosome
<input checked="" type="radio"/>	D. Cell membrane
<input type="radio"/>	E. Mitochondria

Next question

G protein-coupled receptors span the cell membrane

### Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

Ligand-gated ion channel

- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

Tyrosine kinase receptors

- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors

- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors

- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

**Question 90 of 402**

Next

A study looks at whether golf actually increases the risk of medial epicondylitis. Sixty people who regularly play golf are matched to sixty people who do not play golf. Thirty of the golfers had developed medial epicondylitis at some point compared to ten of the non-golfers.

What is the odds ratio of developing medial epicondylitis for people who play golf?

- ☐ A. 0.3
- ☐ B. 3
- ☐ C. 5
- ☐ D. 2.5
- ☐ E. 3.33

Next question

Remember to calculate the odds, rather than risk, initially:

Odds of a golfer developing medial epicondylitis =  $30 / 30 = 1$

Odds a non-golfer developing medial epicondylitis =  $10 / 50 = 0.2$

The odds ratio is therefore =  $1 / 0.2 = 5$

**Odds and odds ratio**

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome. The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control.

Odds ratios are the usual reported measure in case-control studies. It approximates to relative risk if the outcome of interest is rare.

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Achieved = 50% pain relief
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol =  $40 / 20 = 2$

The odds of achieving significant pain relief with placebo =  $30 / 60 = 0.5$

Therefore the odds ratio =  $2 / 0.5 = 4$

A 54-year-old woman is treated with rituximab for non-Hodgkin's lymphoma. What is the target of rituximab?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. CD20  |
| <input type="radio"/> | B. CD52  |
| <input type="radio"/> | C. Epidermal growth factor receptor            |
| <input type="radio"/> | D. CD22  |
| <input type="radio"/> | E. Vascular endothelial growth factor receptor |

Next question

Rituximab - monoclonal antibody against CD20

### Monoclonal antibodies

Monoclonal antibodies have an increasing role in medicine. They are manufactured by a technique called somatic cell hybridization. This involves the fusion of myeloma cells with spleen cells from a mouse that has been immunized with the desired antigen. The resulting fused cells are termed a hybridoma and act as a 'factory' for producing monoclonal antibodies. The main limitation to this is that mouse antibodies are immunogenic leading to the formation of human anti-mouse antibodies (HAMAs). This problem is overcome by combining the variable region from the mouse body with the constant region from a human antibody.

Clinical examples of monoclonal antibodies:

- infliximab (anti-TNF): used in rheumatoid arthritis and Crohn's
- rituximab (anti-CD20): used in non-Hodgkin's lymphoma and rheumatoid arthritis
- cetuximab (anti epidermal growth factor receptor): used in metastatic colorectal cancer and head and neck cancer
- trastuzumab (anti-HER2, an EGF receptor): used in metastatic breast cancer
- alemtuzumab (anti-CD52): used in chronic lymphocytic leukaemia
- abciximab (anti-glycoprotein IIb/IIIa receptor): prevention of ischaemic events in patients undergoing percutaneous coronary interventions
- OKT3 (anti-CD3): used to prevent organ rejection

Monoclonal antibodies are also used for:

- medical imaging when combined with a radioisotope
- identification of cell surface markers in biopsied tissue
- diagnosis of viral infections

A 25-year-old man who has been morbidly obese for the past five years is reviewed in the endocrinology clinic. In this patient, which one of the following hormones would increase appetite as levels increase?

<input type="radio"/>	A. Leptin
<input type="radio"/>	B. Thyroxine
<input type="radio"/>	C. Adiponectin
<input type="radio"/>	D. Ghrelin
<input type="radio"/>	E. Serotonin

[Next question](#)

#### Obesity hormones

- **Leptin** Lowers appetite
- **Ghrelin** Gains appetite

Whilst thyroxine can increase appetite it does not fit with the clinical picture being described

#### Obesity: physiology

##### Leptin

Leptin is thought to play a key role in the regulation of body weight. It is produced by adipose tissue and acts on satiety centres in the hypothalamus and decreases appetite. More adipose tissue (e.g. in obesity) results in high leptin levels.

Leptin stimulates the release of melanocyte-stimulating hormone (MSH) and corticotrophin-releasing hormone (CRH). Low levels of leptin stimulates the release of neuropeptide Y (NPY)

##### Ghrelin

Where as leptin induces satiety, ghrelin stimulates hunger. It is produced mainly by the fundus of the stomach and the pancreas. Ghrelin levels increase before meals and decrease after meals

A 50-year-old man is reviewed in the neurology clinic. For the past four months he has been experiencing problems with his right shoulder. On examination he has weakness of shoulder abduction and to a lesser extent weak elbow flexion. A small patch of numbness is noted over the deltoid muscle but otherwise sensation is normal. Where is the neurological lesion?

- |                       |       |
|-----------------------|-------|
| <input type="radio"/> | A. C4 |
| <input type="radio"/> | B. C5 |
| <input type="radio"/> | C. C6 |
| <input type="radio"/> | D. C7 |
| <input type="radio"/> | E. C8 |

[Next question](#)

This man has weakness of both the deltoid (C5, C6) and the biceps muscle (C5, C6, C7). The location of the sensory loss points to a C5 lesion however

### Upper limb anatomy

The information below contains selected facts which commonly appear in examinations:

#### Deltoid muscle

- supplied by the axillary nerve (C5,C6)
- actions: mainly shoulder abduction



**Question 94 of 402**

Next

Which one of the following is in direct anatomical contact with the left kidney?

- ☐ A. Stomach
- ☐ B. Distal part of small intestine
- ☐ C. Spleen
- ☐ D. Pancreas
- ☐ E. Duodenum

Next question

**Renal anatomy**

The tables below show the anatomical relations of the kidneys:

Right kidney

Direct contact	Layer of peritoneum in-between
Right suprarenal gland Duodenum Colon	Liver Distal part of small intestine

Left kidney

Direct contact	Layer of peritoneum in-between
Left suprarenal gland Pancreas Colon	Stomach Spleen Distal part of small intestine

Which one of the following statements regarding relative risk is correct?

- ☐ A. Relative risk = 1 - absolute risk reduction
- ☐ B. It is the usual outcome measure of cohort studies
- ☐ C. Risk may be defined as the odds of an outcome happening
- ☐ D. Relative risk = 1 / odds ratio
- ☐ E. If the risk ratio is less than 1 then the rate of an event is increased compared to controls

Next question

Remember that risk and odds are different. If 20 patients die out of every 100 who have a myocardial infarction then the risk of dying is  $20 / 100 = 0.2$  whereas the odds are  $20 / 80 = 0.25$ .

### Relative risk

**Relative risk (RR)** is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER). The term relative risk ratio is sometimes used instead of relative risk.

To recap

- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Experienced significant pain relief
Paracetamol	100	60
Placebo	80	20

Experimental event rate,  $EER = 60 / 100 = 0.6$

Control event rate,  $CER = 20 / 80 = 0.25$

Therefore the relative risk ratio =  $EER / CER = 0.6 / 0.25 = 2.4$

If the risk ratio is  $> 1$  then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is  $< 1$  then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

**Relative risk reduction (RRR)** or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate

Using the above data,  $RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140\%$

The parents of a 3-year-old boy with cystic fibrosis ask for advice. They are considering having more children. What is the chance that their next child will be a carrier of the cystic fibrosis gene?

- |                       |            |
|-----------------------|------------|
| <input type="radio"/> | A. 50%     |
| <input type="radio"/> | B. 100%    |
| <input type="radio"/> | C. 1 in 25 |
| <input type="radio"/> | D. 25%     |
| <input type="radio"/> | E. 66.6%   |

[Next question](#)

As cystic fibrosis is an autosomal recessive condition there is a 50% chance that their next child will be a **carrier** of cystic fibrosis (i.e. be heterozygous for the genetic defect) and a 25% chance that the child will actually have the disease (be homozygous).

### Cystic fibrosis

Cystic fibrosis (CF) is an autosomal recessive disorder causing increased viscosity of secretions (e.g. lungs and pancreas). It is due to a defect in the cystic fibrosis transmembrane conductance regulator gene (CFTR), which codes a cAMP-regulated chloride channel

In the UK 80% of CF cases are due to delta F508 on the long arm of chromosome 7. Cystic fibrosis affects 1 per 2500 births, and the carrier rate is c. 1 in 25

Organisms which may colonise CF patients

- Staph aureus
- *Pseudomonas aeruginosa*
- Burkholderia cepacia\*
- Aspergillus

\*previously known as *Pseudomonas cepacia*

What does troponin T bind to?

- ☐ A. Tropomyosin
- ☐ B. Actin in thin myofilaments
- ☐ C. Protein kinase C inhibitors
- ☐ D. Calcium ions
- ☐ E. T-tubule membrane wall

Next question

Tropomyosin is a protein which regulates actin. It associates with actin in muscle fibres and regulates muscle contraction by regulating the binding of myosin.

### Cardiac enzymes and protein markers

Interpretation of the various cardiac enzymes has now largely been superseded by the introduction of troponin T and I. Questions still however commonly appear in the MRCP

Key points for the exam

- myoglobin is the first to rise
- CK-MB is useful to look for reinfarction as it returns to normal after 2-3 days (troponin T remains elevated for up to 10 days)

	Begins to rise	Peak value	Returns to normal
<b>Myoglobin</b>	1-2 hours	6-8 hours	1-2 days
<b>CK-MB</b>	2-6 hours	16-20 hours	2-3 days
<b>CK</b>	4-8 hours	16-24 hours	3-4 days
<b>Trop T</b>	4-6 hours	12-24 hours	7-10 days
<b>AST</b>	12-24 hours	36-48 hours	3-4 days
<b>LDH</b>	24-48 hours	72 hours	8-10 days

Acute intermittent porphyria is due to a defect in:

<input type="radio"/>	A. ALA synthetase
<input type="radio"/>	B. PPG oxidase
<input type="radio"/>	C. Uroporphyrinogen decarboxylase
<input type="radio"/>	D. Ferrochelatase
<input type="radio"/>	E. Porphobilinogen deaminase

Next question

AIP - porphobilinogen deAminase; PCT - uroporphyrinogen deCarboxylase

## Porphyrias

### Overview

- abnormality in enzymes responsible for the biosynthesis of haem
- results in overproduction of intermediate compounds (porphyrins)
- may be acute or non-acute

### Acute intermittent porphyria (AIP)

- autosomal dominant
- defect in porphobilinogen deaminase
- female and 20-40 year olds more likely to be affected
- typically present with abdominal symptoms, neuropsychiatric symptoms
- hypertension and tachycardia common
- urine turns deep red on standing

### Porphyria cutanea tarda (PCT)

- most common hepatic porphyria
- defect in uroporphyrinogen decarboxylase
- may be caused by hepatocyte damage e.g. alcohol, oestrogens
- classically photosensitive rash with bullae, skin fragility on face and dorsal aspect of hands
- urine: elevated uroporphyrinogen and pink fluorescence of urine under Wood's lamp
- manage with chloroquine

## Variegate porphyria

- autosomal dominant
- defect in protoporphyrinogen oxidase
- photosensitive blistering rash
- abdominal and neurological symptoms
- more common in South Africans

Which one of the following pathophysiological changes is most responsible for emphysema?

<input type="radio"/>	A. Mucosal oedema and mucus plugging
<input type="radio"/>	B. Destruction of alveolar walls secondary to proteinases
<input type="radio"/>	C. Airway hypersensitivity
<input type="radio"/>	D. Smooth muscle contraction
<input type="radio"/>	E. Hypertrophy of mucous secreting glands

Next question

Proteinases such as elastase cause irreversible damage to the supporting connective tissue of the alveolar septa. Smoking accelerates this process.

#### COPD: causes

Smoking!

Alpha-1 antitrypsin deficiency

Other causes

- cadmium (used in smelting)
- coal
- cotton
- cement
- grain



A 17-year-old man is investigated for recurrent infections and easy bruising. In the past year he has had four episodes of pneumonia. Other than the bruising he is noted to have severe eczema on his trunk and arms. A full blood count is ordered and reported as follows:

Hb	14.1 g/dl
Plt	$82 \times 10^9/l$
WBC	$5.9 \times 10^9/l$
Neuts	$4.4 \times 10^9/l$

Further bloods show low immunoglobulin M levels. What is the most likely diagnosis?

- ☐ A. Bruton's congenital agammaglobulinaemia
- ☐ B. Wiskott-Aldrich syndrome
- ☐ C. Ataxic telangiectasia
- ☐ D. Chediak-Higashi syndrome
- ☐ E. DiGeorge syndrome

Next question

#### Wiskott-Aldrich syndrome

- recurrent bacterial infections (e.g. Chest)
- eczema
- thrombocytopaenia

#### Wiskott-Aldrich syndrome

Wiskott-Aldrich syndrome causes primary immunodeficiency due to a combined B- and T-cell dysfunction. It is inherited in a X-linked recessive fashion and is thought to be caused by mutation in the WASP gene.

#### Features

- recurrent bacterial infections (e.g. Chest)
- eczema
- thrombocytopaenia
- low IgM levels

A study is to be performed to assess whether the combined oral contraceptive pill is protective against pelvic inflammatory disease. What is the most appropriate type of study design to provide robust evidence?

- ☐ A. Cohort study
- ☐ B. Placebo-controlled randomised controlled trial
- ☐ C. Case-control study
- ☐ D. Cross-sectional survey
- ☐ E. Cross-over trial

[Next question](#)

Whilst a case-control study may be used it would provide inferior evidence to that of a cohort study. It is of course not ethical to give women placebo contraceptive pills, as would be required with a randomised control trial

### Study design

The following table highlights the main features of the main types of study:

<b>Randomised controlled trial</b>	<p>Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo)</p> <p>Practical or ethical problems may limit use</p>
<b>Cohort study</b>	<p>Observational and prospective. Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome.</p> <p>The usual outcome measure is the relative risk.</p> <p>Examples include Framingham Heart Study</p>
<b>Case-control study</b>	<p>Observational and retrospective. Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition.</p> <p>The usual outcome measure is the odds ratio.</p> <p>Inexpensive, produce quick results Useful for studying rare conditions Prone to confounding</p>
<b>Cross-sectional survey</b>	<p>Provide a 'snapshot', sometimes called prevalence studies</p> <p>Provide weak evidence of cause and effect</p>

Which of the following may be used in the treatment of hereditary angioedema?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Anabolic steroids       |
| <input type="radio"/> | B. Oral contraceptive pill |
| <input type="radio"/> | C. ACE inhibitors          |
| <input type="radio"/> | D. Beta-blockers           |
| <input type="radio"/> | E. Aspirin                 |

Next question

### Hereditary angioedema

Hereditary angioedema is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

#### Investigation

- C1-INH level is low during an attack
- low C2 and C4 levels are seen, even between attacks. Serum C4 is the most reliable and widely used screening tool

#### Symptoms

- attacks may be preceded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

#### Management

- acute: IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help

Which of the following conditions is inherited in a X-linked recessive fashion?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Androgen insensitivity syndrome |
| <input type="radio"/> | B. Myotonic dystrophy              |
| <input type="radio"/> | C. von Willebrand's disease        |
| <input type="radio"/> | D. Ehlers-Danlos syndrome          |
| <input type="radio"/> | E. Huntington's disease            |

Next question

X-linked conditions: Duchenne/Becker, haemophilia, G6PD

### X-linked recessive conditions

The following conditions are inherited in a X-linked recessive fashion:

Androgen insensitivity syndrome  
Becker muscular dystrophy  
Colour blindness  
Duchenne muscular dystrophy  
Fabry's disease  
G6PD deficiency  
Haemophilia A,B  
Hunter's disease  
Lesch-Nyhan syndrome  
Nephrogenic diabetes insipidus  
Ocular albinism  
Retinitis pigmentosa  
Wiskott-Aldrich syndrome

The following diseases have varying patterns of inheritance, with the majority being in an X-linked recessive fashion:

Chronic granulomatous disease (in > 70%)

Which one of the following statements regarding hypersensitivity reactions is false?

<input type="radio"/>	A. Delayed hypersensitivity is responsible for graft versus host disease
<input type="radio"/>	B. Anaphylaxis is a type I reaction
<input type="radio"/>	C. Type II reactions are caused by circulating antibodies reacting with antigen on cell surface
<input type="radio"/>	D. Type IV reactions are T cell mediated
<input type="radio"/>	E. Goodpasture's syndrome is an example of a type III reaction

Goodpasture's syndrome is actually an example of a type II reaction. The other statements are true

### Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

#### Type I - Anaphylactic

- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

#### Type II - Cell bound

- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

#### Type III - Immune complex

- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

#### Type IV - Delayed hypersensitivity

- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

#### Type V - Stimulated hypersensitivity

- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

Which one of the following best describes the Bohr effect?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Increase in pO <sub>2</sub> means CO <sub>2</sub> binds less well to Hb      |
| <input type="radio"/> | B. Decreasing acidity (or pCO <sub>2</sub> ) means oxygen binds less well to Hb |
| <input type="radio"/> | C. Decrease in pO <sub>2</sub> means CO <sub>2</sub> binds less well to Hb      |
| <input type="radio"/> | D. Raised 2,3-DPG enhances oxygen delivery to the tissues                       |
| <input type="radio"/> | E. Increasing acidity (or pCO <sub>2</sub> ) means oxygen binds less well to Hb |

Next question

## Respiratory physiology

Chloride shift

- CO<sub>2</sub> diffuses into RBCs
- CO<sub>2</sub> + H<sub>2</sub>O  $\xrightarrow{\text{carbonic anhydrase}}$  HCO<sub>3</sub><sup>-</sup> + H<sup>+</sup>
- H<sup>+</sup> combines with Hb
- HCO<sub>3</sub><sup>-</sup> diffuses out of cell, - Cl<sup>-</sup> replaces it

Bohr effect

- increasing acidity (or pCO<sub>2</sub>) means O<sub>2</sub> binds less well to Hb

Haldane effect

- increase pO<sub>2</sub> means CO<sub>2</sub> binds less well to Hb

**Question 106 of 402**

Next

A new drug is trialled for the treatment of lung cancer. Drug A is given to 500 people with early stage non-small cell lung cancer and a placebo is given to 450 people with the same condition. After 5 years 300 people who received drug A had survived compared to 225 who received the placebo. What is the number needed to treat to save one life?

- ☐ A. 3.33
- ☐ B. 75
- ☐ C. 10
- ☐ D. 5
- ☐ E. 2

Next question

$$\text{NNT} = 1 / \text{Absolute Risk Reduction}$$

The question asks about the number needed to treat to save one life. The 'event' is therefore survival.

Experimental (drug A) event rate =  $300 / 500 = 0.6$

Control (placebo) event rate =  $225 / 450 = 0.5$

Absolute risk reduction =  $0.6 - 0.5 = 0.1$

Number needed to treat =  $1 / 0.1 = 10$

**Numbers needed to treat and absolute risk reduction**

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by  $1/(\text{Absolute risk reduction})$  and is rounded to the next highest whole number

Experimental event rate (EER) = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate (CER) = (Number who had particular outcome with the control/ (Total number who had the control)

**Absolute risk reduction = CER-EER or EER-CER?**

The absolute risk reduction (ARR) may be calculated by finding the absolute difference between the control event rate (CER) and the experimental event rate (EER). You will often find both versions of the above listed in different sources. In some ways it doesn't matter which you use as you will end up with the same answer but from a technical point of view:

- if the outcome of the study is undesirable then  $ARR = CER - EER$
- if the outcome of the study is desirable then  $ARR^* = EER - CER$

\*this may be more accurately termed absolute benefit increase, rather than absolute risk reduction



A 34-year-old man is climbing Mount Kilimanjaro. For the past two days he has complained of nausea and a headache. The climbing team is now at an altitude of 4,500m when he develops shortness of breath and a pink frothy cough. Examination reveals bibasal crackles. What is the most appropriate treatment, other than descent?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Nifedipine                     |
| <input type="radio"/> | B. Frusemide                      |
| <input type="radio"/> | C. Mannitol                       |
| <input type="radio"/> | D. Hydralazine                    |
| <input type="radio"/> | E. Third-generation cephalosporin |

[Next question](#)

This man has developed high altitude pulmonary oedema (HAPE) and should to be treated with prompt descent, oxygen and nifedipine if it is available. Other options for treating HAPE include dexamethasone, acetazolamide and phosphodiesterase type V inhibitors.

### Altitude related disorders

There are three main types of altitude related disorders: acute mountain sickness (AMS), which may progress to high altitude pulmonary edema (HAPE) or high altitude cerebral edema (HACE). All three conditions are due to the chronic hypobaric hypoxia which develops at high altitudes

Acute mountain sickness is generally a self-limiting condition. Features of AMS start to occur above 2,500 - 3,000m, developing gradually over 6-12 hours and potentially last a number of days:

- headache
- nausea
- fatigue

### Prevention and treatment of AMS

- the risk of AMS may actually be positively correlated to physical fitness
- gain altitude at no more than 500 m per day
- acetazolamide (a carbonic anhydrase inhibitor) is widely used to prevent AMS and has a supporting evidence base
- treatment: descent

A minority of people above 4,000m go onto develop high altitude pulmonary oedema (HAPE) or high altitude cerebral oedema (HACE), potentially fatal conditions

- HAPE presents with classical pulmonary oedema features
- HACE presents with headache, ataxia, papilloedema

## Management of HACE

- descent
- dexamethasone

## Management of HAPE

- descent
- nifedipine, dexamethasone, acetazolamide, phosphodiesterase type V inhibitors\*
- oxygen if available

\*the relative merits of these different treatments has only been studied in small trials. All seem to work by reducing systolic pulmonary artery pressure

What is the main mechanism by which vitamin B12 is absorbed?

- |                                  |  |
|----------------------------------|--|
| <input type="radio"/>            | A. Passive absorption in the terminal ileum                    |
| <input type="radio"/>            | B. Active absorption in the middle to terminal part of jejunum |
| <input type="radio"/>            | C. Active absorption by the parietal cells of the stomach      |
| <input checked="" type="radio"/> | D. Active absorption in the terminal ileum                     |
| <input type="radio"/>            | E. Passive absorption in the proximal ileum                    |

Next question

Vitamin B12 is actively absorbed in the terminal ileum

A small amount of vitamin B12 is passively absorbed without being bound to intrinsic factor.

### Vitamin B12 deficiency

Vitamin B12 is mainly used in the body for red blood cell development and also maintenance of the nervous system. It is absorbed after binding to intrinsic factor (secreted from parietal cells in the stomach) and is actively absorbed in the terminal ileum. A small amount of vitamin B12 is passively absorbed without being bound to intrinsic factor.

#### Causes of vitamin B12 deficiency

- pernicious anaemia
- post gastrectomy
- poor diet
- disorders of terminal ileum (site of absorption): Crohn's, blind-loop etc

#### Features of vitamin B12 deficiency

- macrocytic anaemia
- sore tongue and mouth
- neurological symptoms: e.g. Ataxia
- neuropsychiatric symptoms: e.g. Mood disturbances

#### Management

- if no neurological involvement 1 mg of IM hydroxocobalamin 3 times each week for 2 weeks, then once every 3 months
- if a patient is also deficient in folic acid then it is important to treat the B12 deficiency first to avoid precipitating subacute combined degeneration of the cord

For a patient undergoing an elective splenectomy, when is the optimal time to give the pneumococcal vaccine?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Four weeks before surgery        |
| <input type="radio"/> | B. One week before surgery          |
| <input type="radio"/> | C. Immediately following surgery    |
| <input type="radio"/> | D. Two weeks after surgery          |
| <input type="radio"/> | E. At least one month after surgery |

Next question

The current British National Formulary recommends giving the vaccine at least 2 weeks before elective splenectomy. Therefore 4 weeks is the best response from the given options.

### Splenectomy

Following a splenectomy patients are particularly at risk from pneumococcus, Haemophilus, meningococcus and Capnocytophaga canimorsus\* infections

#### Vaccination

- if elective, should be done 2 weeks prior to operation
- Hib, meningitis A & C
- annual influenza vaccination
- pneumococcal vaccine every 5 years

#### Antibiotic prophylaxis

- penicillin V: unfortunately clear guidelines do not exist of how long antibiotic prophylaxis should be continued. It is generally accepted though that penicillin should be continued for at least 2 years and at least until the patient is 16 years of age, although the majority of patients are usually put on antibiotic prophylaxis for life

\*usually from dog bites

A 20-year-old man is admitted to the Emergency Department with chest pain. He confides that he has snorted 'a large amount' of cocaine in the previous hours. Which one of the following features is his cocaine use most likely to cause?

<input type="radio"/>	A. Hypokalaemia
<input type="radio"/>	B. Hyperthermia
<input type="radio"/>	C. Decreased deep tendon reflexes
<input type="radio"/>	D. Hypotension
<input type="radio"/>	E. Metabolic alkalosis

## Cocaine

Cocaine use may cause a wide variety of adverse effects

### Cardiovascular effects

- myocardial infarction
- both tachycardia and bradycardia may occur
- hypertension
- QRS widening and QT prolongation
- aortic dissection

### Neurological effects

- seizures
- mydriasis
- hypertonia
- hyperreflexia

### Psychiatric effects

- agitation
- psychosis
- hallucinations

### Others

- hyperthermia
- metabolic acidosis
- rhabdomyolysis

Which one of the following types of thyroid cancer is associated with the RET oncogene?

- ☐ A. Anaplastic
- ☐ B. Lymphoma
- ☐ C. Follicular
- ☒ D. Medullary
- ☐ E. All types of thyroid cancer

Next question

The RET oncogene encodes a receptor tyrosine kinase and is associated with MEN type 2.

Papillary thyroid cancer also appears to be associated with the RET oncogene

### Multiple endocrine neoplasia

The table below summarises the three main types of multiple endocrine neoplasia (MEN)

MEN type I	MEN type IIa	MEN type IIb
<p>Mnemonic 'three P's':</p> <p>parathyroid (95%): hyperparathyroidism due to parathyroid hyperplasia</p> <p>pituitary (70%)</p> <p>pancreas (50%, e.g. insulinoma, gastrinoma)</p> <p>also: adrenal and thyroid</p>	<p>phaeochromocytoma</p> <p>medullary thyroid cancer (70%)</p> <p>parathyroid (60%)</p>	<p>medullary thyroid cancer</p> <p>phaeochromocytoma</p> <p>marfanoid body habitus</p> <p>neuromas</p>
<p>MEN1 gene</p> <p>Most common presentation = hypercalcaemia</p>	<p>RET oncogene</p>	<p>RET oncogene</p>

MEN is inherited as an autosomal dominant disorder

Which of the following statements is true regarding the p53 gene?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. It is an oncogene  |
| <input type="radio"/> | B. Mutation results in a gain of function                                     |
| <input type="radio"/> | C. 50% of families with a strong history of breast cancer have a p53 mutation |
| <input type="radio"/> | D. Li-Fraumeni syndrome predisposes to the development of sarcomas            |
| <input type="radio"/> | E. It is located on chromosome 13   |

Next question

## p53

p53 is a tumour suppressor gene located on chromosome 17p. It is the most commonly mutated gene in breast, colon and lung cancer

p53 is thought to play a crucial role in the cell cycle, preventing entry into the S phase until DNA has been checked and repaired. It may also be a key regulator of apoptosis

**Li-Fraumeni syndrome** is a rare autosomal dominant disorder characterised by the early onset of a variety of cancers such as sarcomas and breast cancer. It is caused by mutation in the p53 gene

A 38-year-old woman comes for review. Six months ago she fractured her left wrist whilst skiing. The fracture was treated using a cast and repeat x-rays showed that the bone had healed well. Unfortunately for the past few weeks she has been plagued with ongoing 'shooting pains' in her left hand associated with swelling. On examination the left hand is extremely tender to even light touch. Her left hand is also slightly swollen compared to the right. What is the most likely diagnosis?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Depression                     |
| <input type="radio"/> | B. Conversion disorder            |
| <input type="radio"/> | C. Complex regional pain syndrome |
| <input type="radio"/> | D. Ulnar nerve injury             |
| <input type="radio"/> | E. Osteomyelitis                  |

[Next question](#)

### Complex regional pain syndrome

Complex regional pain syndrome (CRPS) is the modern, umbrella term for a number of conditions such as reflex sympathetic dystrophy and causalgia. It describes a number of neurological and related symptoms which typically occur following surgery or a minor injury. CRPS is 3 times more common in women.

There are two types of CRPS:

- type I (most common): there is no demonstrable lesion to a major nerve
- type II: there is a lesion to a major nerve

#### Features

- progressive, disproportionate symptoms to the original injury/surgery
- allodynia
- temperature and skin colour changes
- oedema and sweating
- motor dysfunction
- the Budapest Diagnostic Criteria are commonly used in the UK

#### Management

- early physiotherapy is important
- neuropathic analgesia in-line with NICE guidelines
- specialist management (e.g. Pain team) is required



### Question 114 of 402

Next

A new blood test to screen patients for heart failure is trialled on 500 patients. The test was positive in 40 of the 50 patients shown to have heart failure by echocardiography. It was also positive in 20 patients who were shown not to have heart failure. What is the positive predictive value of the test?

- ☐ A. 0.8
- ☐ B. 0.66
- ☐ C. 0.33
- ☐ D. 0.1
- ☐ E. Cannot be calculated

Next question

A contingency table can be constructed from the above data, as shown below:

	Heart failure	No heart failure
Test positive	40	20
Test negative	10	430

Positive predictive value =  $TP / (TP + FP) = 40 / (40 + 20) = 0.66$

### Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	$TP / (TP + FN)$	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	$TN / (TN + FP)$	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	$TP / (TP + FP)$	The chance that the patient has the condition if the diagnostic test is positive
<b>Negative predictive value</b>	$TN / (TN + FN)$	The chance that the patient does not have the condition if the diagnostic test is negative

<b>Likelihood ratio for a positive test result</b>	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
<b>Likelihood ratio for a negative test result</b>	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

What are funnel plots primarily used for?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Demonstrate the heterogeneity of a meta-analysis  |
| <input type="radio"/> | B. Demonstrate the existence of publication bias in meta-analyses  |
| <input type="radio"/> | C. Provide a graphical representation of the relative risk results in a case-control study                     |
| <input type="radio"/> | D. Provide a graphical representation of the relative risk results in a cohort study                           |
| <input type="radio"/> | E. Provide a graphical representation of the probability of a patient experiencing a particular adverse effect |

Next question

Funnel plots - show publication bias in meta-analyses

### Funnel plot

A funnel plot is primarily used to demonstrate the existence of publication bias in meta-analyses. Funnel plots are usually drawn with treatment effects on the horizontal axis and study size on the vertical axis.

#### Interpretation

- a symmetrical, inverted funnel shape indicates that publication bias is unlikely
- conversely, an asymmetrical funnel indicates a relationship between treatment effect and study size. This indicates either publication bias or a systematic difference between smaller and larger studies ('small study effects')

Which one of the following is the most common cause of recurrent first trimester spontaneous miscarriage?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Factor V Leiden gene mutation |
| <input type="radio"/> | B. Polycystic ovarian syndrome   |
| <input type="radio"/> | C. Hyperprolactinaemia           |
| <input type="radio"/> | D. Antithrombin III deficiency   |
| <input type="radio"/> | E. Antiphospholipid syndrome     |

Next question

Antiphospholipid antibodies (aPL) are present in 15% of women with recurrent miscarriage, but in comparison, the prevalence of aPL in women with a low risk obstetric history is less than 2%

### Antiphospholipid syndrome: pregnancy

Antiphospholipid syndrome is an acquired disorder characterised by a predisposition to both venous and arterial thromboses, recurrent fetal loss and thrombocytopenia. It may occur as a primary disorder or secondary to other conditions, most commonly systemic lupus erythematosus (SLE)

In pregnancy the following complications may occur:

- recurrent miscarriage
- IUGR
- pre-eclampsia
- placental abruption
- pre-term delivery
- venous thromboembolism

### Management

- low-dose aspirin should be commenced once the pregnancy is confirmed on urine testing
- low molecular weight heparin once a fetal heart is seen on ultrasound. This is usually discontinued at 34 weeks gestation
- these interventions increase the live birth rate seven-fold

Which foramen does the maxillary nerve go through?

- ☐ A. Jugular foramen
- ☐ B. Foramen ovale
- ☐ C. Superior orbital fissure
- ☐ D. Optic canal
- ☐ E. Foramen rotundum

Next question

### Foramina of the skull

Questions asking about foramina of the skull have come up in the exam in previous years. Below is a brief summary of the major foramina, please see the Wikipedia link for a full list.

Foramen	Bone	Vessels	Nerves
Optic canal	Sphenoid	Ophthalmic artery	Optic nerve (II)
Superior orbital fissure	Sphenoid	Superior ophthalmic vein Inferior ophthalmic vein	Oculomotor nerve (III) Trochlear nerve (IV) lacrimal, frontal and nasociliary branches of ophthalmic nerve (V1) Abducent nerve (VI)
Inferior orbital fissure	Sphenoid and maxilla	Inferior ophthalmic veins Infraorbital artery Infraorbital vein	Zygomatic nerve and infraorbital nerve of maxillary nerve (V2) Orbital branches of pterygopalatine ganglion
Foramen rotundum	Sphenoid	-	Maxillary nerve (V2)
Foramen ovale	Sphenoid	Accessory meningeal artery	Mandibular nerve (V3)
Jugular foramen	Occipital and temporal	Posterior meningeal artery Ascending pharyngeal artery Inferior petrosal sinus Sigmoid sinus Internal jugular vein	Glossopharyngeal nerve (IX) Vagus nerve (X) Accessory nerve (XI)

A 59-year-old man presents with a severe pain deep within his right ear. He feels dizzy and reports that the room 'is spinning'. Clinical examination shows a partial facial nerve palsy on the right side and vesicular lesions on the anterior two-thirds of his tongue. What is the most likely diagnosis?

<input type="radio"/>	A. Meniere's disease
<input type="radio"/>	B. Herpes zoster ophthalmicus
<input type="radio"/>	C. Ramsay Hunt syndrome
<input type="radio"/>	D. Acoustic neuroma
<input type="radio"/>	E. Trigeminal neuralgia

[Next question](#)

### Ramsay Hunt syndrome

Ramsay Hunt syndrome (herpes zoster oticus) is caused by the reactivation of the varicella zoster virus in the geniculate ganglion of the seventh cranial nerve.

#### Features

- auricular pain is often the first feature
- facial nerve palsy
- vesicular rash around the ear
- other features include vertigo and tinnitus

#### Management

- oral aciclovir and corticosteroids are usually given

Which layer of the epidermis are melanocytes found in?

- ☐ A. Stratum lucidum
- ☒ B. Stratum germinativum
- ☐ C. Stratum spinosum
- ☐ D. Stratum corneum
- ☐ E. Stratum granulosum

Next question

Epidermis - 5 layers - bottom layer = stratum germinativum which gives rise to keratinocytes and contains melanocytes

## Epidermis

The epidermis is the outermost layer of the skin and is composed of a stratified squamous epithelium with an underlying basal lamina

It may be divided in to five layers:

Layer	Description
Stratum corneum	Flat, dead, scale-like cells filled with keratin Continually shed
Stratum lucidum	Clear layer - present in thick skin only
Stratum granulosum	Cells form links with neighbours
Stratum spinosum	Squamous cells begin keratin synthesis Thickest layer of epidermis
Stratum germinativum	The basement membrane - single layer of columnar epithelial cells Gives rise to keratinocytes Contains melanocytes

Which one of the following foods is the best source of folic acid?

<input type="radio"/>	A. Cheese
<input type="radio"/>	B. Red meat
<input type="radio"/>	C. Liver
<input type="radio"/>	D. Fish
<input type="radio"/>	E. Milk

[Next question](#)

Folic acid is also present in green vegetables and nuts

### Folate metabolism

Drugs which interfere with metabolism

- trimethoprim
- methotrexate
- pyrimethamine

Drugs which can reduce absorption

- phenytoin



Which one of the following defines the standard error of the mean?

- |                                  |  |
|----------------------------------|--|
| <input type="radio"/>            | A. Square root (Standard deviation / number of patients) |
| <input type="radio"/>            | B. Number of patients / square root (mean)               |
| <input type="radio"/>            | C. Number of patients / square root (standard deviation) |
| <input checked="" type="radio"/> | D. Standard deviation / square root (number of patients) |
| <input type="radio"/>            | E. Standard deviation / square root (mean)               |

Next question

Standard error of the mean = standard deviation / square root (number of patients)

### Standard error of the mean

The standard error of the mean (SEM) is a measure of the spread expected for the mean of the observations - i.e. how 'accurate' the calculated sample mean is from the true population mean

Key point

- $SEM = SD / \text{square root } (n)$
- where SD = standard deviation and n = sample size

Therefore the SEM gets smaller as the sample size (n) increases

A confidence interval for the mean can be calculated in a similar way to that for a single observation, i.e. The 95% confidence interval:

- lower limit = mean - (1.96 \* SEM)
- upper limit = mean + (1.96 \* SEM)

A 24-year-old man is investigated for visual loss and is diagnosed as having Leber's optic atrophy. Given the mitochondrial inheritance of this condition, which one of the following relatives is most likely to be also affected?

<input type="radio"/>	A. Daughter
<input type="radio"/>	B. Sister
<input type="radio"/>	C. Son
<input type="radio"/>	D. Paternal uncle
<input type="radio"/>	E. Father

[Next question](#)

Mitochondrial diseases follow a maternal inheritance pattern

All the children of an affected mother will inherit a mitochondrial condition. His sister will therefore also be affected.

### Mitochondrial diseases

Whilst most DNA is found in the cell nucleus, a small amount of double-stranded DNA is present in the mitochondria. It encodes protein components of the respiratory chain and some special types of RNA

Mitochondrial inheritance has the following characteristics:

- inheritance is only via the maternal line as the sperm contributes no cytoplasm to the zygote
- all children of affected males will not inherit the disease
- all children of affected females will inherit it
- generally encode rare neurological diseases
- poor genotype:phenotype correlation - within a tissue or cell there can be different mitochondrial populations - this is known as heteroplasmy)

### Histology

- muscle biopsy classically shows 'red, ragged fibres' due to increased number of mitochondria

Examples include:

- Leber's optic atrophy
- MELAS syndrome: mitochondrial encephalomyopathy lactic acidosis and stroke-like episodes
- MERRF syndrome: myoclonus epilepsy with ragged-red fibres
- Kearns-Sayre syndrome: onset in patients < 20 years old, external ophthalmoplegia, retinitis pigmentosa. Ptosis may be seen
- sensorineural hearing loss

You review a patient in the respiratory clinic who has a history of recurrent pulmonary embolism despite anticoagulation with warfarin. Which one of the following physiological changes would be expected?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Increased lung compliance     |
| <input type="radio"/> | B. Reduced TLCO                  |
| <input type="radio"/> | C. Reduced forced vital capacity |
| <input type="radio"/> | D. Reduced FEV1                  |
| <input type="radio"/> | E. Increased FEV1 / FVC ration   |

[Next question](#)

### Transfer factor

The transfer factor describes the rate at which a gas will diffuse from alveoli into blood. Carbon monoxide is used to test the rate of diffusion. Results may be given as the total gas transfer (TLCO) or that corrected for lung volume (transfer coefficient, KCO)

#### Causes of a raised TLCO

- asthma
- pulmonary haemorrhage (Wegener's, Goodpasture's)
- left-to-right cardiac shunts
- polycythaemia
- hyperkinetic states
- male gender, exercise

#### Causes of a lower TLCO

- pulmonary fibrosis
- pneumonia
- pulmonary emboli
- pulmonary oedema
- emphysema
- anaemia
- low cardiac output

KCO also tends to increase with age. Some conditions may cause an increased KCO with a normal or reduced TLCO

- pneumonectomy/lobectomy
- scoliosis/kyphosis
- neuromuscular weakness
- ankylosis of costovertebral joints e.g. ankylosing spondylitis

A 24-year-old female who is 10 weeks in to her first pregnancy presents for review. Her blood pressure today is 126/82 mmHg. What normally happens to blood pressure during pregnancy?

- ☐ A. Falls in first half of pregnancy before rising to pre-pregnancy levels before term
- ☐ B. Systolic + diastolic rises by < 10 mmHg
- ☐ C. Systolic + diastolic falls by < 10 mmHg
- ☐ D. Rise in first half of pregnancy before falling to pre-pregnancy levels before term
- ☐ E. Doesn't change

[Next question](#)

## Hypertension in pregnancy

The classification of hypertension in pregnancy is complicated and varies. Remember, in normal pregnancy:

- blood pressure usually falls in the first trimester (particularly the diastolic), and continues to fall until 20-24 weeks
- after this time the blood pressure usually increases to pre-pregnancy levels by term

Hypertension in pregnancy is usually defined as:

- systolic > 140 mmHg or diastolic > 90 mmHg
- or an increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic

After establishing that the patient is hypertensive they should be categorised into one of the following groups

Pre-existing hypertension	Pregnancy-induced hypertension (PIH, also known as gestational hypertension)	Pre-eclampsia
<p>A history of hypertension before pregnancy or an elevated blood pressure &gt; 140/90 mmHg before 20 weeks gestation</p> <p>No proteinuria, no oedema</p> <p>Occurs in 3-5% of pregnancies and is more common in older women</p>	<p>Hypertension (as defined above) occurring in the second half of pregnancy (i.e. after 20 weeks)</p> <p>No proteinuria, no oedema</p> <p>Occurs in around 5-7% of pregnancies</p> <p>Resolves following birth (typically after one month). Women with PIH are at increased risk of future pre-eclampsia or hypertension later in life</p>	<p>Pregnancy-induced hypertension in association with proteinuria (&gt; 0.3g / 24 hours)</p> <p>Oedema may occur but is now less commonly used as a criteria</p> <p>Occurs in around 5% of pregnancies</p>

One of your colleagues confides in you that he has just been diagnosed with hepatitis B. He has not told anyone else as he is worried he may lose his job. He is currently working as a general surgeon in the local hospital. You try to persuade him to inform occupational health but he refuses. What is the most appropriate action?

- |                                  |  |
|----------------------------------|--|
| <input type="radio"/>            | A. Keep confidentiality but ask him to stop taking blood |
| <input type="radio"/>            | B. Send an anonymous letter to his employer              |
| <input type="radio"/>            | C. Keep confidentiality                                  |
| <input checked="" type="radio"/> | D. Inform your colleague's employing body                |
| <input type="radio"/>            | E. Contact the police                                    |

[Next question](#)

Whilst this may seem harsh patient safety has to be paramount. Please see the updated GMC guidelines for further details.

#### **GMC guidance: confidentiality**

We will not try to replicate the extensive guidance given by the General Medical Council here. There is a link available for more detailed information.

Which one of the following may be used to calculate the number needed to treat?

- ☐ A.  $1 / (\text{Absolute risk reduction})$
- ☐ B.  $(\text{Absolute Risk Reduction}) / (\text{Number of people in trial})$
- ☐ C.  $((\text{Control event rate}) - (\text{Experimental event rate})) / (\text{Control event rate})$
- ☐ D.  $1 / (\text{Relative risk})$
- ☐ E.  $1 / (\text{Hazard ratio})$

Next question

$$\text{NNT} = 1 / \text{Absolute Risk Reduction}$$

### Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by  $1/(\text{Absolute risk reduction})$  and is rounded to the next highest whole number

Experimental event rate (EER) =  $(\text{Number who had particular outcome with the intervention}) / (\text{Total number who had the intervention})$

Control event rate (CER) =  $(\text{Number who had particular outcome with the control}) / (\text{Total number who had the control})$

### Absolute risk reduction = CER-EER or EER-CER?

The absolute risk reduction (ARR) may be calculated by finding the absolute difference between the control event rate (CER) and the experimental event rate (EER). You will often find both versions of the above listed in different sources. In some ways it doesn't matter which you use as you will end up with the same answer but from a technical point of view:

- if the outcome of the study is undesirable then  $\text{ARR} = \text{CER} - \text{EER}$
- if the outcome of the study is desirable then  $\text{ARR}^* = \text{EER} - \text{CER}$

\*this may be more accurately termed absolute benefit increase, rather than absolute risk reduction

What level of evidence does a randomised control trial offer?

<input type="radio"/>	A.	Ia
<input type="radio"/>	B.	Ib
<input type="radio"/>	C.	IIa
<input type="radio"/>	D.	IIb
<input type="radio"/>	E.	IV

Next question

### Study design: evidence and recommendations

#### Levels of evidence

- Ia - evidence from meta-analysis of randomised controlled trials
- Ib - evidence from at least one randomised controlled trial
- IIa - evidence from at least one well designed controlled trial which is not randomised
- IIb - evidence from at least one well designed experimental trial
- III - evidence from case, correlation and comparative studies
- IV - evidence from a panel of experts

#### Grading of recommendation

- Grade A - based on evidence from at least one randomised controlled trial (i.e. Ia or Ib)
- Grade B - based on evidence from non-randomised controlled trials (i.e. IIa, IIb or III)
- Grade C - based on evidence from a panel of experts (i.e. IV)

A 67-year-old woman presents with lethargy, depression and constipation. A set of screening blood tests reveals the following:

Calcium	3.05 mmol/l
Albumin	41 g/l

What is the single most useful test for determining the cause of her hypercalcaemia?

- ☐ A. ESR
- ☐ B. Phosphate
- ☐ C. Vitamin D level
- ☐ D. Parathyroid hormone
- ☐ E. ACE level

Next question

Parathyroid hormone levels are useful as malignancy and primary hyperparathyroidism are the two most common causes of hypercalcaemia. A parathyroid hormone that is normal or raised suggests primary hyperparathyroidism.

### Hypercalcaemia: causes

The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

- sarcoidosis\*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, calcium containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone\*\*

\*other causes of granulomas may lead to hypercalcaemia e.g. Tuberculosis and histoplasmosis

\*\*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation



Which one of the following is only secreted by the adrenal medulla?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Noradrenaline |
| <input type="radio"/> | B. Aldosterone   |
| <input type="radio"/> | C. Metadrenaline |
| <input type="radio"/> | D. Cortisol      |
| <input type="radio"/> | E. Adrenaline    |

Next question

### Adrenal medulla

The adrenal medulla secretes virtually all the adrenaline in the body as well as secreting small amounts of noradrenaline. It essentially represents an enlarged and specialised sympathetic ganglion

At which point in the menstrual cycle do progesterone levels peak?

- ☐ A. Luteal phase
- ☐ B. Ovulation
- ☐ C. Follicular phase
- ☐ D. Levels remain constant throughout cycle
- ☐ E. Menstruation

Progesterone is secreted by the corpus luteum following ovulation.

### Menstrual cycle

The menstrual cycle may be divided into the following phases:

	Days
<b>Menstruation</b>	1-4
<b>Follicular phase (proliferative phase)</b>	5-13
<b>Ovulation</b>	14
<b>Luteal phase (secretory phase)</b>	15-28

Further details are given in the table below

	Follicular phase (proliferative phase)	Luteal phase (secretory phase)
<b>Ovarian histology</b>	A number of follicles develop.  One follicle will become dominant around the mid-follicular phase	Corpus luteum
<b>Endometrial histology</b>	Proliferation of endometrium	Endometrium changes to secretory lining under influence of progesterone
<b>Hormones</b>	A rise in FSH results in the development of follicles which in turn secrete oestradiol  When the egg has matured, it secretes enough oestradiol to trigger the acute release of LH. This in turn leads to ovulation	Progesterone secreted by corpus luteum rises through the luteal phase.  If fertilisation does not occur the corpus luteum will degenerate and progesterone levels fall  Oestradiol levels also rise again during the luteal phase
<b>Cervical mucus</b>	Following menstruation the mucus is thick and forms a plug across the external os  Just prior to ovulation the mucus becomes clear, acellular, low viscosity. It also becomes 'stretchy' - a quality termed spinnbarkeit	Under the influence of progesterone it becomes thick, scant, and tacky
<b>Basal body temperature</b>	Falls prior to ovulation due to the influence of oestradiol	Rises following ovulation in response to higher progesterone levels

**Question 131 of 402**

Next

A 23-year-old female with Down's syndrome is reviewed in clinic. Which one of the following features is least associated with her condition?

<input type="radio"/>	A. Infertility
<input type="radio"/>	B. Hypothyroidism
<input type="radio"/>	C. Alzheimer's disease
<input type="radio"/>	D. Short stature
<input type="radio"/>	E. Ventricular septal defect

Next question

As this patient is female she is likely to be subfertile rather than infertile - please see the notes below

**Down syndrome: features**

## Clinical features

- face: upslanting palpebral fissures, epicanthic folds, Brushfield spots in iris, protruding tongue, small ears, round/flat face
- flat occiput
- single palmar crease, pronounced 'sandal gap' between big and first toe
- hypotonia
- congenital heart defects (40-50%, see below)
- duodenal atresia
- Hirschsprung's disease

## Cardiac complications

- multiple cardiac problems may be present
- endocardial cushion defect (c. 40%, also known as atrioventricular septal canal defects)
- ventricular septal defect (c. 30%)
- secundum atrial septal defect (c. 10%)
- tetralogy of Fallot (c. 5%)
- isolated patent ductus arteriosus (c. 5%)

## Later complications

- subfertility: males are almost always infertile due to impaired spermatogenesis. Females are usually subfertile, and have an increased incidence of problems with pregnancy and labour
- learning difficulties

- short stature
- repeated respiratory infections (+hearing impairment from glue ear)
- acute lymphoblastic leukaemia
- hypothyroidism
- Alzheimer's
- atlantoaxial instability

**Question 132 of 402**[Next](#)

How many protein-coding genes does a haploid human genome contain?

- |                       |    |           |
|-----------------------|----|-----------|
| <input type="radio"/> | A. | 50,000    |
| <input type="radio"/> | B. | 25,000    |
| <input type="radio"/> | C. | 275,000   |
| <input type="radio"/> | D. | 10,000    |
| <input type="radio"/> | E. | 3 billion |

[Next question](#)

Human genome - 25,000 protein-coding genes

**Human genome**

The human genome is stored on 23 chromosome pairs. The haploid human genome has a total of 3 billion DNA base pairs, making up an estimated 20,000-25,000 protein-coding genes

Which of the following conditions is inherited in an autosomal dominant fashion?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Familial Mediterranean Fever |
| <input type="radio"/> | B. Homocystinuria               |
| <input type="radio"/> | C. Tuberose sclerosis           |
| <input type="radio"/> | D. Ataxia telangiectasia        |
| <input type="radio"/> | E. Friedreich's ataxia          |

Next question

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

### Autosomal dominant conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal dominant:

- Achondroplasia
- Acute intermittent porphyria
- Adult polycystic disease
- Antithrombin III deficiency
- Ehlers-Danlos syndrome
- Familial adenomatous polyposis
- Hereditary haemorrhagic telangiectasia
- Hereditary spherocytosis
- Hereditary non-polyposis colorectal carcinoma
- Huntington's disease
- Hyperlipidaemia type II
- Hypokalaemic periodic paralysis
- Malignant hyperthermia
- Marfan's syndromes

- Myotonic dystrophy
- Neurofibromatosis
- Noonan syndrome
- Osteogenesis imperfecta
- Peutz-Jeghers syndrome
- Retinoblastoma
- Romano-Ward syndrome
- Tuberose sclerosis
- Von Hippel-Lindau syndrome
- Von Willebrand's disease\*

\*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

A 72-year-old woman is admitted for investigation of hyponatraemia. Which one of the following features is most consistent with the syndrome of inappropriate ADH secretion?

<input type="radio"/>	A. Peripheral oedema
<input type="radio"/>	B. Recent lisinopril therapy
<input type="radio"/>	C. Urine osmolality of 325 mmol/kg
<input type="radio"/>	D. Serum sodium of 115 mmol/l
<input type="radio"/>	E. Urinary sodium of 40 mmol/l

[Next question](#)

## Hyponatraemia

Hyponatraemia may be caused by water excess or sodium depletion. Causes of pseudohyponatraemia include hyperlipidaemia (increase in serum volume) or a taking blood from a drip arm. Urinary sodium and osmolality levels aid making a diagnosis

### Urinary sodium > 20 mmol/l

Sodium depletion, renal loss (patient often hypovolaemic)

- diuretics
- Addison's
- diuretic stage of renal failure

Patient often euvolaemic

- SIADH (urine osmolality > 500 mmol/kg)
- hypothyroidism

### Urinary sodium < 20 mmol/l

Sodium depletion, extra-renal loss

- diarrhoea, vomiting, sweating
- burns, adenoma of rectum

Water excess (patient often hypervolaemic and oedematous)

- secondary hyperaldosteronism: CCF, cirrhosis
- reduced GFR: renal failure
- IV dextrose, psychogenic polydipsia



**Question 135 of 402**

Next

A study looks at the benefits of adding a new antiplatelet drug to aspirin following a myocardial infarction. The following results are obtained:

	Percentage of patients having further MI within 3 months
Aspirin	4%
Aspirin + new drug	3%

What is the number needed to treat to prevent one patient having a further myocardial infarction within 3 months?

- ☐ A. 0.75
- ☐ B. 0.33
- ☐ C. Cannot calculate without more data
- ☐ D. 1
- ☐ E. 100

Next question

$$\text{NNT} = 1 / \text{Absolute Risk Reduction}$$

$$\text{NNT} = 1 / (\text{control event rate} - \text{experimental event rate})$$

$$= 1 / (0.04 - 0.03) = 1 / (0.01) = 100$$

**Numbers needed to treat and absolute risk reduction**

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by  $1/(\text{Absolute risk reduction})$  and is rounded to the next highest whole number

Experimental event rate (EER) = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate (CER) = (Number who had particular outcome with the control / (Total number who had the control)

**Absolute risk reduction = CER-EER or EER-CER?**

The absolute risk reduction (ARR) may be calculated by finding the absolute difference between the control event rate (CER) and the experimental event rate (EER). You will often find both versions of the above listed in different sources. In some ways it doesn't matter which you use as you will end up with the same answer but from a technical point of view:

- if the outcome of the study is undesirable then  $ARR = CER - EER$
- if the outcome of the study is desirable then  $ARR^* = EER - CER$

\*this may be more accurately termed absolute benefit increase, rather than absolute risk reduction

Which one of the following features is least likely to be seen in a patient with pellagra?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Diarrhoea  |
| <input type="radio"/> | B. Depression |
| <input type="radio"/> | C. Dysphagia  |
| <input type="radio"/> | D. Dermatitis |
| <input type="radio"/> | E. Dementia   |

Next question

Depression is quite a common early finding in patients with pellagra

### Pellagra

Pellagra is caused by nicotinic acid (niacin) deficiency. The classical features are the 3 D's - dermatitis, diarrhoea and dementia

Pellagra may occur as a consequence of isoniazid therapy (isoniazid inhibits the conversion of tryptophan to niacin) and it is more common in alcoholics.

#### Features

- dermatitis (brown scaly rash on sun-exposed sites - termed Casal's necklace if around neck)
- diarrhoea
- dementia, depression
- death if not treated

Which of the following conditions is inherited in an autosomal recessive fashion?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Familial adenomatous polyposis |
| <input type="radio"/> | B. Noonan syndrome                |
| <input type="radio"/> | C. Malignant hyperthermia         |
| <input type="radio"/> | D. Antithrombin III deficiency    |
| <input type="radio"/> | E. Congenital adrenal hyperplasia |

[Next question](#)

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

### Autosomal recessive conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal recessive:

- Albinism
- Ataxia telangiectasia
- Congenital adrenal hyperplasia
- Cystic fibrosis
- Cystinuria
- Familial Mediterranean Fever
- Fanconi anaemia
- Friedreich's ataxia
- Gilbert's syndrome\*
- Glycogen storage disease
- Haemochromatosis
- Homocystinuria
- Lipid storage disease: Tay-Sach's, Gaucher, Niemann-Pick
- Mucopolysaccharidoses: Hurler's

- PKU
- Sickle cell anaemia
- Thalassaemias
- Wilson's disease

\*this is still a matter of debate and many textbooks will list Gilbert's as autosomal dominant

Southern blotting is used to:

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Amplify RNA                  |
| <input type="radio"/> | B. Detect DNA                   |
| <input type="radio"/> | C. Detect RNA                   |
| <input type="radio"/> | D. Detect and quantify proteins |
| <input type="radio"/> | E. Amplify DNA                  |

Next question

#### Molecular biology techniques

- SNOW (South - **N**Orth - **W**est)
- DROP (**D**NNA - **R**NA - **P**rotein)

#### Molecular biology techniques

The following table shows a very basic summary of molecular biology techniques

Southern blotting	Detects DNA
Northern blotting	Detects RNA
Western blotting	Detects and quantifies proteins

Which of the following is not a tumour suppressor gene?

<input type="radio"/>	A. p53
<input type="radio"/>	B. APC
<input type="radio"/>	C. NF-1
<input type="radio"/>	D. Rb
<input type="radio"/>	E. myc

[Next question](#)

myc is an oncogene which encodes a transcription factor

### Tumour suppressor genes

#### Basics

- genes which normally control the cell cycle
- exhibit a recessive effect - both copies must be mutated before cancer occurs

#### Examples

Gene	Associated cancers
p53	Common to many cancers, Li-Fraumeni syndrome
APC	Colorectal cancer
BRCA1	Breast and ovarian cancer
BRCA2	Breast and ovarian cancer
NF1	Neurofibromatosis
Rb	Retinoblastoma
WT1	Wilm's tumour
Multiple tumor suppressor 1 (MTS-1, p16)	Melanoma

A 23-year-old student is investigated following an anaphylactic reaction suspected to be secondary to a wasp sting. Which one of the following is the most appropriate first-line test to investigate the cause of the reaction?

- ☐ A. Hair analysis
- ☐ B. Radioallergosorbent test (RAST)
- ☐ C. Desensitization therapy
- ☐ D. Skin patch test
- ☐ E. Skin prick test

[Next question](#)

Given the history of anaphylaxis it would not be appropriate to perform a skin prick test

### Allergy tests

<b>Skin prick test</b>	<p>Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes</p> <p>Useful for food allergies and also pollen</p>
<b>Radioallergosorbent test (RAST)</b>	<p>Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive)</p> <p>Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom</p> <p>Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines</p>
<b>Skin patch testing</b>	<p>Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The patches are removed 48 hours later with the results being read by a dermatologist after a further 48 hours</p>



Which one of the following best describes the main action of the polymerase chain reaction?

- |                                  |                                 |
|----------------------------------|---------------------------------|
| <input type="radio"/>            | A. DNA identification using RNA |
| <input checked="" type="radio"/> | B. DNA amplification            |
| <input type="radio"/>            | C. RNA translation to protein   |
| <input type="radio"/>            | D. RNA amplification            |
| <input type="radio"/>            | E. DNA to RNA conversion        |

Next question

## PCR

Polymerase chain reaction (PCR) is a molecular genetic investigation technique. The main advantage of PCR is its sensitivity: only one strand of sample DNA is needed to detect a particular DNA sequence. It now has many uses including prenatal diagnosis, detection of mutated oncogenes and diagnosis of infections. PCR is also extensively used in forensics. Prior to the procedure it is necessary to have two DNA oligonucleotide primers. These are complimentary to specific DNA sequences at either end of the target DNA

Initial prep

- sample of DNA is added to test tube along with two DNA primers
- a thermostable DNA polymerase (Taq) is added

The following cycle then takes place

- mixture is heated to almost boiling point causing denaturing (uncoiling) of DNA
- mixture is the allowed to cool: complimentary strands of DNA pair up, as there is an excess of the primer sequences they pair with DNA preferentially

The above cycle is then repeated, with the amount of DNA doubling each time

Reverse transcriptase PCR

- used to amplify RNA
- RNA is converted to DNA by reverse transcriptase
- gene expression in the form of mRNA (rather than the actually DNA sequence) can therefore be analyzed

Which one of the following would cause a fall in the carbon monoxide transfer factor (TLCO)?

- ☐ A. Acute asthma
- ☐ B. Wegener's granulomatosis
- ☐ C. Polycythaemia
- ☐ D. Exercise
- ☐ E. Emphysema

Next question

#### Transfer factor

- raised: asthma, haemorrhage, left-to-right shunts, polycythaemia
- low: everything else

#### Transfer factor

The transfer factor describes the rate at which a gas will diffuse from alveoli into blood. Carbon monoxide is used to test the rate of diffusion. Results may be given as the total gas transfer (TLCO) or that corrected for lung volume (transfer coefficient, KCO)

##### Causes of a raised TLCO

- asthma
- pulmonary haemorrhage (Wegener's, Goodpasture's)
- left-to-right cardiac shunts
- polycythaemia
- hyperkinetic states
- male gender, exercise

##### Causes of a lower TLCO

- pulmonary fibrosis
- pneumonia
- pulmonary emboli
- pulmonary oedema
- emphysema
- anaemia
- low cardiac output

KCO also tends to increase with age. Some conditions may cause an increased KCO with a normal or reduced TLCO

- pneumonectomy/lobectomy
- scoliosis/kyphosis
- neuromuscular weakness
- ankylosis of costovertebral joints e.g. ankylosing spondylitis

In which one of the following conditions is intravenous immunoglobulin therapy most likely to be beneficial?

<input type="radio"/>	A. Graves' ophthalmopathy
<input type="radio"/>	B. Kawasaki disease
<input type="radio"/>	C. Inclusion body myositis
<input type="radio"/>	D. Multiple sclerosis
<input type="radio"/>	E. Rheumatoid arthritis

Next question

### Immunoglobulins: therapeutics

The Department of Health issued guidelines on the use of intravenous immunoglobulins in May 2008

#### Uses

- primary and secondary immunodeficiency
- idiopathic thrombocytopenic purpura
- myasthenia gravis
- Guillain-Barre syndrome
- Kawasaki disease
- toxic epidermal necrolysis
- pneumonitis induced by CMV following transplantation
- low serum IgG levels following haematopoietic stem cell transplant for malignancy
- dermatomyositis
- chronic inflammatory demyelinating polyradiculopathy

#### Basics

- formed from large pool of donors (e.g. 5,000)
- IgG molecules with a subclass distribution similar to that of normal blood
- half-life of 3 weeks

A 37-year-old woman who has a BMI of 44 kg/m<sup>2</sup> undergoes a Roux-en-Y gastric bypass. Of which vitamin/mineral is she most likely to require supplementation?

<input type="radio"/>	A. Vitamin C
<input type="radio"/>	B. Iron
<input type="radio"/>	C. Folic acid
<input type="radio"/>	D. Zinc
<input type="radio"/>	E. Vitamin B6

[Next question](#)

The duodenum is the primary site of absorption for both iron and calcium. All gastric bypass operations bypass the duodenum. Nearly all menstruating women will therefore require iron supplementation.

### Obesity: bariatric surgery

The use of bariatric surgery in the management of obesity has developed significantly over the past decade. It is now recognised that for many obese patients who fail to lose weight with lifestyle and drug interventions the risks and expense of long-term obesity outweigh those of surgery.

#### NICE guidelines on bariatric surgery for adults

Consider surgery for people with severe obesity if:

- they have a BMI of 40 kg/m<sup>2</sup> or more, or between 35 kg/m<sup>2</sup> and 40 kg/m<sup>2</sup> and other significant disease (for example, type 2 diabetes mellitus, hypertension) that could be improved if they lost weight
- all appropriate non-surgical measures have failed to achieve or maintain adequate clinically beneficial weight loss for at least 6 months
- they are receiving or will receive intensive specialist management
- they are generally fit for anaesthesia and surgery
- they commit to the need for long-term follow-up

Consider surgery as a first-line option for adults with a BMI of more than 50 kg/m<sup>2</sup> in whom surgical intervention is considered appropriate; consider orlistat before surgery if the waiting time is long

Types of bariatric surgery:

- primarily restrictive: laparoscopic-adjustable gastric banding (LAGB) or sleeve gastrectomy
- primarily malabsorptive: classic biliopancreatic diversion (BPD) has now largely been replaced by biliopancreatic diversion with duodenal switch
- mixed: Roux-en-Y gastric bypass surgery

Which operation?

- LAGB produces less weight loss than malabsorptive or mixed procedures but as it has fewer complications it is normally the first-line intervention in patients with a BMI of 30-39kg/m<sup>2</sup>
- patients with a BMI > 40 kg/m<sup>2</sup> may be considered for a gastric bypass or sleeve gastrectomy. The latter may be done as a sole procedure or as an initial procedure prior to bypass
- primarily malabsorptive procedures are usually reserved for very obese patients (e.g. BMI > 60 kg/m<sup>2</sup>)

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Next

A study is performed looking at the chance of stroke in high-risk patients taking a new oral antithrombotic drug compared to warfarin. The following results are obtained:

	Total number of patients	Number who had a stroke within a 3 year period
New drug	200	10
Warfarin	600	12

What is the relative risk of having a stroke within a 3 year period for patients taking the new drug compared to warfarin?

- ☐ A. 3.33
- ☐ B. 0.66
- ☐ C. 1.2
- ☐ D. 2.5
- ☐ E. Cannot calculate from above data

Next question

Relative risk = EER / CER

Experimental event rate, EER =  $10 / 200 = 0.05$

Control event rate, CER =  $12 / 600 = 0.02$

Therefore the relative risk =  $EER / CER = 0.05 / 0.02 = 2.5$

**Relative risk**

**Relative risk (RR)** is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER). The term relative risk ratio is sometimes used instead of relative risk.

To recap

- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Experienced significant pain relief
--	--------------------------	-------------------------------------

<b>Paracetamol</b>	100	60
<b>Placebo</b>	80	20

Experimental event rate,  $EER = 60 / 100 = 0.6$

Control event rate,  $CER = 20 / 80 = 0.25$

Therefore the relative risk ratio =  $EER / CER = 0.6 / 0.25 = 2.4$

If the risk ratio is  $> 1$  then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is  $< 1$  then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

**Relative risk reduction (RRR)** or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate

Using the above data,  $RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140\%$

A 67-year-old man presents with shortness-of-breath. He has a past history of aortic stenosis but is otherwise well. On examination he has a systolic murmur and a clear chest. Routine bloods are as follows:

Hb	8.7 g/dl
MCV	71 fl
Plt	$277 \times 10^9/l$
WBC	$6.4 \times 10^9/l$

Which one of the following investigations is most likely to explain his anaemia?

<input type="radio"/>	A. Colonoscopy
<input type="radio"/>	B. Renal biopsy
<input type="radio"/>	C. Duodenal biopsy
<input type="radio"/>	D. Gastroscopy
<input type="radio"/>	E. Echocardiogram

Next question

This patient most likely has angiodysplasia which has a known association with aortic stenosis.

### Angiodysplasia

Angiodysplasia is a vascular deformity of the gastrointestinal tract which predisposes to bleeding and iron deficiency anaemia. There is thought to be an association with aortic stenosis, although this is debated. Angiodysplasia is generally seen in elderly patients

#### Diagnosis

- colonoscopy
- mesenteric angiography if acutely bleeding

#### Management

- endoscopic cautery or argon plasma coagulation
- antifibrinolytics e.g. Tranexamic acid
- oestrogens may also be used



Which one of the following statements best describes a type I statistical error?

- ☐ A. The null hypothesis is rejected when it is true
- ☐ B. The null hypothesis is accepted when it is false
- ☐ C. The p value fails to reach statistical significance
- ☐ D. The alternative hypothesis is rejected when it is true
- ☐ E. A study fails to reach an appropriate power

Next question

### Significance tests

A null hypothesis ( $H_0$ ) states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct.

For example:

- 'there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not'

The alternative hypothesis ( $H_1$ ) is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

The **p value** is the probability of obtaining a result by chance at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. It is therefore equal to the chance of making a type I error (see below).

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist, a false positive. This is determined against a preset significance level (termed alpha). As the significance level is determined in advance the chance of making a type I error is not affected by sample size. It is however increased if the number of end-points are increased. For example if a study has 20 end-points it is likely one of these will be reached, just by chance.
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists, a false negative. The probability of making a type II error is termed beta. It is determined by both sample size and alpha

	Study accepts $H_0$	Study rejects $H_0$
Reality $H_0$		Type 1 error (alpha)
Reality $H_1$	Type 2 error (beta)	Power (1 - beta)

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false, i.e. the probability of detecting a statistically significant difference

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Which one of the following statements regarding the standard error of the mean is correct?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Is the square root of standard deviation                                 |
| <input type="radio"/> | B. It is independent of sample size   |
| <input type="radio"/> | C. Is a measure of correlation between two variables                        |
| <input type="radio"/> | D. Confidence intervals cannot be applied to the standard error of the mean |
| <input type="radio"/> | E. Gets smaller as the sample size increases                                |

Next question

### Standard error of the mean

The standard error of the mean (SEM) is a measure of the spread expected for the mean of the observations - i.e. how 'accurate' the calculated sample mean is from the true population mean

Key point

- $SEM = SD / \text{square root } (n)$
- where SD = standard deviation and n = sample size

Therefore the SEM gets smaller as the sample size (n) increases

A confidence interval for the mean can be calculated in a similar way to that for a single observation, i.e. The 95% confidence interval:

- lower limit = mean - (1.96 \* SEM)
- upper limit = mean + (1.96 \* SEM)

Which one of the following hormones is under continuous inhibition?

<input type="radio"/>	A. Growth hormone
<input type="radio"/>	<b>B. Prolactin</b>
<input type="radio"/>	C. Gonadotropin releasing hormone
<input type="radio"/>	D. Thyroid releasing hormone
<input type="radio"/>	E. Adrenocorticotrophic hormone

Next question

Prolactin - under continuous inhibition

Prolactin is unique amongst the pituitary hormones in being tonically inhibited by the hypothalamus

### Prolactin and galactorrhoea

Prolactin is secreted by the anterior pituitary gland with release being controlled by a wide variety of physiological factors. Dopamine acts as the primary prolactin releasing inhibitory factor and hence dopamine agonists such as bromocriptine may be used to control galactorrhoea. It is important to differentiate the causes of galactorrhoea (due to the actions of prolactin on breast tissue) from those of gynaecomastia

Features of excess prolactin

- men: impotence, loss of libido, galactorrhoea
- women: amenorrhoea, galactorrhoea

Causes of raised prolactin

- prolactinoma
- pregnancy
- oestrogens
- physiological: stress, exercise, sleep
- acromegaly: 1/3 of patients
- polycystic ovarian syndrome
- primary hypothyroidism (due to thyrotrophin releasing hormone (TRH) stimulating prolactin release)

Drug causes of raised prolactin

- metoclopramide, domperidone
- phenothiazines
- haloperidol
- very rare: SSRIs, opioids

What is the main constituent of pulmonary surfactant?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Apolipoprotein SP-B             |
| <input type="radio"/> | B. Phosphatidylglycerol            |
| <input type="radio"/> | C. Pulmonary elastase              |
| <input type="radio"/> | D. Apolipoprotein SP-A             |
| <input type="radio"/> | E. Dipalmitoyl phosphatidylcholine |

Next question

Pulmonary surfactant - main constituent is **dipalmitoyl phosphatidylcholine (DPPC)**

### Pulmonary surfactant

Surfactant is a mixture of phospholipids, carbohydrates and proteins released by type 2 pneumocytes. The main functioning component is dipalmitoyl phosphatidylcholine (DPPC) which reduces alveolar surface tension.

#### Basics

- first detectable around 28 weeks
- as alveoli decrease in size, surfactant concentration is increased, helping prevent the alveoli from collapsing
- reduces the muscular force needed to expand the lungs (i.e. decreases the work of breathing)
- lowers the elastic recoil at low lung volumes and thus helps to prevent the alveoli from collapsing at the end of each expiration

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Next

Whilst reviewing a patient's drug card you notice that you prescribed the wrong dose of atenolol when the patient was initially clerked. Instead of 25mg atenolol od you prescribed 50mg atenolol od. She has received the incorrect dose on two occasions. On examining Mrs Smith you note her blood pressure and pulse are normal. Mrs Smith has a past history of anxiety and describes herself as a 'worrier'. What is the most appropriate action?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Complete an entry in your e-portfolio  |
| <input type="radio"/> | B. Apologise to the patient + complete a clinical incident form                             |
| <input type="radio"/> | C. Complete a clinical incident form + avoid telling patient to prevent unnecessary anxiety |
| <input type="radio"/> | D. Fill out a 'yellow card'   |
| <input type="radio"/> | E. Keep her on the higher dose as she is suffering no ill effects                           |

Next question

In this scenario the patient appears to have come to no harm following the error. This should not however change your approach to the situation. The patient should be informed of what has happened, an apology should be made and reassurance given that there appears to be no ill effects. By completing a clinical incident form you add to a body of data which may in the long term change to practice.

An entry to your e-portfolio at least shows that you both acknowledge and are willing to learn from the error. The yellow card system is intended to report side-effects from drugs rather than prescription errors and hence is fairly pointless.

The dose of a drug a patient takes should be based on clinical need rather than a reluctance to acknowledge an error.

A 25-year-old man is counselled regarding the genetics of Huntington's disease. Which one of the following best describes the concept of anticipation?

- ☐ A. The psychological effect of a patient knowing they will develop an incurable condition
- ☐ B. Earlier age of onset in successive generations
- ☐ C. More severe disease in successive generations
- ☐ D. Where there is a known history of inherited conditions, patients may attribute symptoms to the onset of the disease
- ☐ E. Screening at risk families to allow early intervention and improve outcomes

[Next question](#)

Anticipation in trinucleotide repeat disorders = **earlier onset** in successive generations

Difficult question. In the exam both B and C were given as choices. The 'classic' definition of anticipation is earlier onset in successive generations. However, in most cases, an increase in the severity of symptoms is also noted. If both options are presented then B should be chosen, as this represents the more accepted definition of anticipation. What do you think?

### Trinucleotide repeat disorders

Trinucleotide repeat disorders are genetic conditions caused by an abnormal number of repeats (expansions) of a repetitive sequence of three nucleotides. These expansions are unstable and may enlarge which may lead to an earlier age of onset in successive generations - a phenomenon known as anticipation\*. In most cases, an increase in the severity of symptoms is also noted

Examples - note dominance of neurological disorders

- Fragile X (CGG)
- Huntington's (CAG)
- myotonic dystrophy (CTG)
- Friedreich's ataxia\* (GAA)
- spinocerebellar ataxia
- spinobulbar muscular atrophy
- dentatorubral pallidoluysian atrophy

\*Friedreich's ataxia is unusual in not demonstrating anticipation

Tamsulosin is a:

<input type="radio"/>	A. Alpha-1b agonist
<input type="radio"/>	B. Alpha-1a agonist
<input type="radio"/>	C. Non-selective alpha antagonist
<input checked="" type="radio"/>	D. Alpha-1a antagonist
<input type="radio"/>	E. Alpha-1b antagonist

Next question

### Adrenoceptor antagonists

Alpha antagonists

- alpha-1: doxazosin
- alpha-1a: tamsulosin - acts mainly on urogenital tract
- alpha-2: yohimbine
- non-selective: phenoxybenzamine (previously used in peripheral arterial disease)

Beta antagonists

- beta-1: atenolol
- non-selective: propranolol

Carvedilol and labetalol are mixed alpha and beta antagonists



A 30-year-old man is referred to ophthalmology due to deteriorating visual acuity. Both his brother and uncle on his mother's side have developed similar problems. What is the most likely mode of inheritance of his condition?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Autosomal dominant  |
| <input type="radio"/> | B. Autosomal recessive |
| <input type="radio"/> | C. X-linked recessive  |
| <input type="radio"/> | D. X-linked dominant   |
| <input type="radio"/> | E. Polygenic           |

[Next question](#)

This first clue is the nature of the disease - many of the inherited eye disorders such as retinitis pigmentosa and ocular albinism are inherited in an x-linked recessive pattern.

For this disorder to be autosomal recessive both the patient's parents would need to be carriers (heterozygous) as well as both his maternal aunt and uncle. Even for common autosomal recessive disorders such as cystic fibrosis the carrier rate is around 1 in 25 making this statistically less likely.

### X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters.

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier.

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen.

A new test to screen for ovarian cancer in patients with a positive family history is tested on 920 patients. The test is positive in 16 of the 20 patients who are proven to have ovarian cancer. Of the remaining patients, only 10 have a positive test. What is the negative predictive value of the new test?

- ☐ A.  $900/920 = 97.8\%$
- ☐ B.  $890/900 = 98.9\%$
- ☐ C.  $10/900 = 1.1\%$
- ☐ D.  $890/894 = 99.6\%$
- ☐ E.  $890/920 = 96.7\%$

Next question

A contingency table can be constructed from the above data, as shown below:

	Ovarian cancer	No ovarian cancer
Test positive	16	10
Test negative	4	890

The negative predictive value =  $TN / (TN + FN) = 890 / (890 + 4) = 890/894$

### Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

Sensitivity	$TP / (TP + FN)$	Proportion of patients with the condition who have a positive test result
Specificity	$TN / (TN + FP)$	Proportion of patients without the condition who have a negative test result
Positive predictive value	$TP / (TP + FP)$	The chance that the patient has the condition if the diagnostic test is positive
Negative predictive value	$TN / (TN + FN)$	The chance that the patient does not have the condition if the diagnostic test is negative

<b>Likelihood ratio for a positive test result</b>	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
<b>Likelihood ratio for a negative test result</b>	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Which one of the following best describes rheumatoid factor?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. IgG against the Fc portion of IgM |
| <input type="radio"/> | B. IgM against the Fc portion of IgA |
| <input type="radio"/> | C. IgM against the Fc portion of IgM |
| <input type="radio"/> | D. IgM against the Fc portion of IgG |
| <input type="radio"/> | E. IgG against the Fc portion of IgA |

Next question

Rheumatoid factor is an IgM antibody against IgG

### Rheumatoid factor

Rheumatoid factor (RF) is a circulating antibody (usually IgM) which reacts with the Fc portion of the patients own IgG

RF can be detected by either

- Rose-Waaler test: sheep red cell agglutination
- Latex agglutination test (less specific)

RF is positive in 70-80% of patients with rheumatoid arthritis, high titre levels are associated with severe progressive disease (but NOT a marker of disease activity)

Other conditions associated with a positive RF include:

- Sjogren's syndrome (around 100%)
- Felty's syndrome (around 100%)
- infective endocarditis (= 50%)
- SLE (= 20-30%)
- systemic sclerosis (= 30%)
- general population (= 5%)
- rarely: TB, HBV, EBV, leprosy

Which one of the following stimulates the release of gastrin from G-cells?

- ☐ A. Histamine
- ☐ B. Somatostatin
- ☐ C. Gastric acid
- ☐ D. Cholecystokinin
- ☐ E. Luminal peptides

[Next question](#)

### Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
<b>Gastrin</b>	G cells in antrum of the stomach	Distension of stomach, vagus nerves (mediated by gastrin-releasing peptide), luminal peptides/amino acids Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
<b>CCK</b>	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
<b>Secretin</b>	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
<b>VIP</b>	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid secretion
<b>Somatostatin</b>	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production

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A 67-year-old woman who is taking long-term prednisolone for polymyalgia rheumatica presents with progressive pain in her right hip joint. A diagnosis of avascular necrosis is suspected. Which investigation is most likely to be diagnostic?

<input type="radio"/>	A. Radionuclide bone scan
<input type="radio"/>	B. MRI
<input type="radio"/>	C. Plain x-ray
<input type="radio"/>	D. CT
<input type="radio"/>	E. DEXA scan

[Next question](#)

In early avascular necrosis a radionuclide bone scan is less sensitive than MRI and the findings may be nonspecific. MRI is therefore the investigation of choice.

**Avascular necrosis**

Avascular necrosis (AVN) may be defined as death of bone tissue secondary to loss of the blood supply. This leads to bone destruction and loss of joint function. It most commonly affects the epiphysis of long bones such as the femur.

**Causes**

- long-term steroid use
- chemotherapy
- alcohol excess
- trauma

**Features**

- initially asymptomatic
- pain in the affected joint

**Investigation**

- plain x-ray findings may be normal initially
- MRI is the investigation of choice. It is more sensitive than radionuclide bone scanning

What is the underlying problem in methaemoglobinaemia?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. The oxidation of Fe <sup>2+</sup> in haemoglobin to Fe <sup>3+</sup> |
| <input type="radio"/> | B. The reduction of Fe <sup>2+</sup> in haemoglobin to Fe <sup>+</sup>  |
| <input type="radio"/> | C. The oxidation of Fe <sup>3+</sup> in haemoglobin to Fe <sup>2+</sup> |
| <input type="radio"/> | D. The reduction of Fe <sup>2+</sup> in haemoglobin to Fe <sup>3+</sup> |
| <input type="radio"/> | E. The reduction of Fe <sup>3+</sup> in haemoglobin to Fe <sup>2+</sup> |

Next question

Methaemoglobinaemia = oxidation of Fe<sup>2+</sup> in haemoglobin to Fe<sup>3+</sup>

### Methaemoglobinaemia

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe<sup>2+</sup> to Fe<sup>3+</sup>. This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe<sup>3+</sup> cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

#### Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

#### Acquired causes

- drugs: sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

#### Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO<sub>2</sub> but decreased oxygen saturation

#### Management

- NADH - methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylene blue if acquired

A 65-year-old Asian female presents with generalised bone pain and muscle weakness. Investigations show:

Calcium	2.07 mmol/l
Phosphate	0.66 mmol/l
ALP	256 U/l

What is the most likely diagnosis?

- ☐ A. Bone tuberculosis
- ☐ B. Hypoparathyroidism
- ☐ C. Myeloma
- ☒ D. Osteomalacia
- ☐ E. Paget's disease

Next question

#### Osteomalacia

- low: calcium, phosphate
- raised: alkaline phosphatase

The low calcium and phosphate combined with the raised alkaline phosphatase point towards osteomalacia

#### Osteomalacia

##### Basics

- normal bony tissue but decreased mineral content
- rickets if when growing
- osteomalacia if after epiphysis fusion

##### Types

- vitamin D deficiency e.g. malabsorption, lack of sunlight, diet
- renal failure
- drug induced e.g. anticonvulsants
- vitamin D resistant; inherited
- liver disease, e.g. cirrhosis



## Features

- rickets: knock-knee, bow leg, features of hypocalcaemia
- osteomalacia: bone pain, fractures, muscle tenderness, proximal myopathy

## Investigation

- low calcium, phosphate, 25(OH) vitamin D
- raised alkaline phosphatase
- x-ray: children - cupped, ragged metaphyseal surfaces; adults - translucent bands (Looser's zones or pseudofractures)

## Treatment

- calcium with vitamin D tablets

Which one of the following statements is not correct regarding hypertension in pregnancy?

- ☐ A. An increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic suggests hypertension
- ☐ B. Pre-eclampsia occurs in around 5% of pregnancies
- ☐ C. Urine dipstick showing protein + is consistent with gestational hypertension
- ☐ D. A rise in blood pressure before 20 weeks suggests pre-existing hypertension
- ☐ E. With gestational hypertension the blood pressure rises in the second half of pregnancy

Next question

Proteinuria suggests pre-eclampsia

### Hypertension in pregnancy

The classification of hypertension in pregnancy is complicated and varies. Remember, in normal pregnancy:

- blood pressure usually falls in the first trimester (particularly the diastolic), and continues to fall until 20-24 weeks
- after this time the blood pressure usually increases to pre-pregnancy levels by term

Hypertension in pregnancy is usually defined as:

- systolic > 140 mmHg or diastolic > 90 mmHg
- or an increase above booking readings of > 30 mmHg systolic or > 15 mmHg diastolic

After establishing that the patient is hypertensive they should be categorised into one of the following groups

Pre-existing hypertension	Pregnancy-induced hypertension (PIH, also known as gestational hypertension)	Pre-eclampsia
<p>A history of hypertension before pregnancy or an elevated blood pressure &gt; 140/90 mmHg before 20 weeks gestation</p> <p>No proteinuria, no oedema</p> <p>Occurs in 3-5% of pregnancies and is more common in older women</p>	<p>Hypertension (as defined above) occurring in the second half of pregnancy (i.e. after 20 weeks)</p> <p>No proteinuria, no oedema</p> <p>Occurs in around 5-7% of pregnancies</p> <p>Resolves following birth (typically after one month). Women with PIH are at increased risk of future pre-eclampsia or hypertension later in life</p>	<p>Pregnancy-induced hypertension in association with proteinuria (&gt; 0.3g / 24 hours)</p> <p>Oedema may occur but is now less commonly used as a criteria</p> <p>Occurs in around 5% of pregnancies</p>

Which one of the following cardiac tissue types has the highest conduction velocity?

- ☐ A. Atrial myocardial tissue
- ☐ B. Ventricular myocardial tissue
- ☐ C. Purkinje fibres
- ☐ D. Atrioventricular node
- ☐ E. Sinoatrial node

Next question

## Electrical activity of the heart

### Myocardial action potential

Phase	Description	Mechanism
0	Rapid depolarisation	Rapid sodium influx These channels automatically deactivate after a few ms
1	Early repolarisation	Efflux of potassium
2	Plateau	Slow influx of calcium
3	Final repolarisation	Efflux of potassium
4	Restoration of ionic concentrations	Resting potential is restored by $\text{Na}^+/\text{K}^+$ ATPase There is slow entry of $\text{Na}^+$ into the cell decreasing the potential difference until the threshold potential is reached, triggering a new action potential

NB cardiac muscle remains contracted 10-15 times longer than skeletal muscle

### Conduction velocity

Atrial conduction	Spreads along ordinary atrial myocardial fibres at 1 m/sec
AV node conduction	0.05 m/sec
Ventricular conduction	Purkinje fibres are of large diameter and achieve velocities of 2-4 m/sec (this allows a rapid and coordinated contraction of the ventricles)

The commonest chromosomal defect in Down's syndrome is:

- ☐ A. Trinucleotide repeat disorder
- ☐ B. Autosomal dominant
- ☐ C. Translocation
- ☐ D. Mosaicism
- ☐ E. Non-dysjunction

Next question

### Down's syndrome: epidemiology and genetics

Risk of Down's syndrome with increasing maternal age

- risk at 30 years = 1/1000
- 35 years = 1/350
- 40 years = 1/100
- 45 years = 1/30

One way of remembering this is by starting at 1/1,000 at 30 years and then dividing the denominator by 3 (i.e. 3 times more common) for every extra 5 years of age

### Cytogenetics

Mode	% of cases	Risk of recurrence
Non-disjunction	94%	1 in 100 if under mother < 35 years
Robertsonian translocation (usually onto 14)	5%	10-15% if mother is translocation carrier 2.5% if father is translocation carrier
Mosaicism	1%	

The chance of a further child with Down's syndrome is approximately 1 in 100 if the mother is less than 35 years old. If the trisomy 21 is a result of a translocation the risk is much higher

What is the site of action of antidiuretic hormone?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Descending loop of Henle   |
| <input type="radio"/> | B. Distal convoluted tubule   |
| <input type="radio"/> | C. Ascending loop of Henle    |
| <input type="radio"/> | D. Proximal convoluted tubule |
| <input type="radio"/> | E. Collecting ducts           |

Next question

Antidiuretic hormone (ADH) - site of action = collecting ducts

### Antidiuretic hormone

Antidiuretic hormone (ADH) is secreted from the posterior pituitary gland. It promotes water reabsorption in the collecting ducts of the kidneys by the insertion of aquaporin-2 channels

Which one of the following diseases is most strongly associated with HLA antigen DR2?

<input type="radio"/>	A. Behcet's disease
<input type="radio"/>	B. Type 1 diabetes mellitus
<input type="radio"/>	C. Coeliac disease
<input type="radio"/>	D. Haemochromatosis
<input type="radio"/>	E. Narcolepsy

Next question

### HLA associations

HLA antigens are encoded for by genes on chromosome 6. HLA A, B and C are class I antigens whilst DP, DQ, DR are class II antigens. Questions are often based around which diseases have strong HLA associations. The most important associations are listed below:

#### HLA-A3

- haemochromatosis

#### HLA-B5

- Behcet's disease

#### HLA-B27

- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

#### HLA-DQ2/DQ8

- coeliac disease

#### HLA-DR2

- narcolepsy
- Goodpasture's

### HLA-DR3

- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

### HLA-DR4

- type 1 diabetes mellitus\*
- rheumatoid arthritis

\*type 1 diabetes mellitus is associated with HLA-DR3 but is more strongly associated with HLA-DR4.

A 25-year-old woman presents for her first cervical smear. What is the most important aetiological factor causing cervical cancer?

<input type="radio"/>	A. Human papilloma virus 6 & 11
<input type="radio"/>	B. Herpes simplex virus 2
<input type="radio"/>	C. Smoking
<input type="radio"/>	D. Combined oral contraceptive pill use
<input type="radio"/>	E. Human papilloma virus 16 & 18

[Next question](#)

Whilst a number of the above are known to contribute to the development of cervical cancer infection with human papilloma virus 16 & 18 is by far the most important factor.

### Cervical cancer

The incidence of cervical cancer peaks around the 6th decade. It may be divided into

- squamous cell cancer (80%)
- adenocarcinoma (20%)

#### Features

- may be detected during routine cervical cancer screening
- abnormal vaginal bleeding: postcoital, intermenstrual or postmenopausal bleeding
- vaginal discharge

#### Risk factors

- human papilloma virus 16,18 & 33
- smoking
- human immunodeficiency virus
- early first intercourse, many sexual partners
- high parity
- lower socioeconomic status
- combined oral contraceptive pill\*

\*the strength of this association is sometimes debated but a large study published in the Lancet (2007 Nov 10;370(9599):1609-21) confirmed the link



**Question 167 of 402**

Next

Which one of the following foodstuffs contains the most calories per unit weight?

<input type="radio"/>	A. White bread
<input type="radio"/>	B. Butter
<input type="radio"/>	C. Pasta
<input type="radio"/>	D. Sugar
<input type="radio"/>	E. Red meat

Next question

**Energy from food**

The amount of energy that may be derived from 1 gram of food is as follows:

- carbohydrates: 4 kcal
- protein: 4 kcal
- fat: 9 kcal

A 24-year-old man is planning an expedition to the Andes. He asks for advice on preventing acute mountain sickness (AMS), other than gradual ascent. What is the most appropriate advice?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Carbonic anhydrase inhibitor                                      |
| <input type="radio"/> | B. Non-steroid anti-inflammatories                                   |
| <input type="radio"/> | C. Ensure maximal physical fitness prior to trip                     |
| <input type="radio"/> | D. Dexamethasone starting 2 days prior to arrival                    |
| <input type="radio"/> | E. There is no evidence of any effective intervention to prevent AMS |

Next question

Acetazolamide, a carbonic anhydrase inhibitor, has an evidence to support its use in preventing AMS. Interestingly, there actually appears to be a positive correlation between physical fitness and the risk of developing AMS

### Altitude related disorders

There are three main types of altitude related disorders: acute mountain sickness (AMS), which may progress to high altitude pulmonary edema (HAPE) or high altitude cerebral edema (HACE). All three conditions are due to the chronic hypobaric hypoxia which develops at high altitudes

Acute mountain sickness is generally a self-limiting condition. Features of AMS start to occur above 2,500 - 3,000m, developing gradually over 6-12 hours and potentially last a number of days:

- headache
- nausea
- fatigue

### Prevention and treatment of AMS

- the risk of AMS may actually be positively correlated to physical fitness
- gain altitude at no more than 500 m per day
- acetazolamide (a carbonic anhydrase inhibitor) is widely used to prevent AMS and has a supporting evidence base
- treatment: descent

A minority of people above 4,000m go onto develop high altitude pulmonary oedema (HAPE) or high altitude cerebral oedema (HACE), potentially fatal conditions

- HAPE presents with classical pulmonary oedema features
- HACE presents with headache, ataxia, papilloedema

## Management of HACE

- descent
- dexamethasone

## Management of HAPE

- descent
- nifedipine, dexamethasone, acetazolamide, phosphodiesterase type V inhibitors\*
- oxygen if available

\*the relative merits of these different treatments has only been studied in small trials. All seem to work by reducing systolic pulmonary artery pressure

Which one of the following causes of primary immunodeficiency is due to a defect in neutrophil function?

<input type="radio"/>	A. Wiskott-Aldrich syndrome
<input type="radio"/>	B. Common variable immunodeficiency
<input type="radio"/>	C. Bruton's congenital agammaglobulinaemia
<input type="radio"/>	D. Di George syndrome
<input type="radio"/>	E. Chronic granulomatous disease

Next question

### Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

#### Neutrophil disorders

- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

#### B-cell disorders

- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

#### T-cell disorders

- DiGeorge syndrome

#### Combined B- and T-cell disorders

- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome

The serum potassium is measured in a 1,000 patients taking an ACE inhibitors. The mean potassium is 4.6 mmol/l with a standard deviation of 0.3 mmol/l. Which one of the following statements is correct?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. 95% of values lie between 4.5 and 4.75 mmol/l   |
| <input type="radio"/> | B. 95.4% of values lie between 4.3 and 4.9 mmol/l  |
| <input type="radio"/> | C. 99.7% of values lie between 4.0 and 5.2 mmol/l  |
| <input type="radio"/> | D. 68.3% of values lie between 4.5 and 4.75 mmol/l |
| <input type="radio"/> | E. 68.3% of values lie between 4.3 and 4.9 mmol/l  |

[Next question](#)

We know that 68.3% of values of a normally distributed variable lie within 1 standard deviation of the mean. This means the range is 4.3 to 4.9 mmol/l.

### Normal distribution

The normal distribution is also known as the Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

#### Properties of the Normal distribution

- symmetrical i.e. Mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 \* SD) to the mean + (1.96 \* SD) is called the 95% confidence interval, i.e. If a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

#### Standard deviation

- the standard deviation (SD) is a measure of how much dispersion exists from the mean
- SD = square root (variance)

**Question 171 of 402**

Next

A 55-year-old man with a history of type 2 diabetes mellitus, bipolar disorder and chronic obstructive pulmonary disease has bloods taken as part of his annual diabetic review:

Na <sup>+</sup>	129 mmol/l
K <sup>+</sup>	3.8 mmol/l
Bicarbonate	24 mmol/l
Urea	3.7 mmol/l
Creatinine	92 µmol/l

Due to his smoking history a chest x-ray is ordered which is reported as normal. Which one of the following medications is most likely to be responsible?

- ☐ A. Metformin
- ☐ B. Lithium
- ☐ C. Carbamazepine
- ☐ D. Sodium valproate
- ☐ E. Pioglitazone

Next question

SIADH - drug causes: carbamazepine, sulfonylureas, SSRIs, tricyclics

Lithium can cause diabetes insipidus but this is generally associated with a high sodium. Lithium only tends to cause raised antidiuretic hormone levels following a severe overdose. Please see the BNF for more details.

**SIADH: causes****Malignancy**

- especially small cell lung cancer
- also: pancreas, prostate

**Neurological**

- stroke
- subarachnoid haemorrhage
- subdural haemorrhage
- meningitis/encephalitis/abscess

## Infections

- tuberculosis
- pneumonia

## Drugs

- sulfonylureas
- SSRIs, tricyclics
- carbamazepine
- vincristine
- cyclophosphamide

## Other causes

- positive end-expiratory pressure (PEEP)
- porphyrias

A cohort study is designed to look at the association between working long hours and blood pressure.

The following results are obtained after 10 years of follow-up:

	Number of patients with normal blood pressure after 10 years	Number of patients diagnosed with hypertension after 10 years	Total
Working < 40 hours/week	1000	50	1,050
Working > 40 hours/week	600	60	660

What is the odds ratio of developing hypertension if you work more than 40 hours/week compared to people who work less than 40 hours/week?

- ☐ A. 60/600
- ☐ B. 0.5
- ☐ C. 2
- ☐ D. 50/60
- ☐ E. 60/50

Next question

The odds of developing hypertension if you work < 40 hours/week is  $50 / 1000 = 1 / 20$  or 0.05

The odds of developing hypertension if you work > 40 hours/week is  $60 / 600 = 1 / 10$  or 0.1

The odds ratio is therefore = (odds of developing hypertension if you work > 40 hours/week) / (odds of developing hypertension if you work < 40 hours/week) =  $0.1/0.05 = 2$

### Odds and odds ratio

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome. The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control.

Odds ratios are the usual reported measure in case-control studies. It approximates to relative risk if the outcome of interest is rare.

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results



	Total number of patients	Achieved = 50% pain relief
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol =  $40 / 20 = 2$

The odds of achieving significant pain relief with placebo =  $30 / 60 = 0.5$

Therefore the odds ratio =  $2 / 0.5 = 4$

Which one of the following statements is true regarding the radial nerve?

<input type="radio"/>	A. Damage at the axilla would lead to wrist drop
<input type="radio"/>	B. Damage at the wrist leads to wasting of the thenar muscles
<input type="radio"/>	C. It supplies the lateral 2 lumbricals
<input type="radio"/>	D. It supplies sensation to the lateral one and a half fingers
<input type="radio"/>	E. It is derived from C6-8 and T1

Next question

## Radial nerve

### Overview

- arises from the posterior cord of the brachial plexus (C5-8)

### Motor to

- extensor muscles (forearm, wrist, fingers, thumb)

### Sensory to

- dorsal aspect of lateral 3 1/2 fingers
- however, only small area between the dorsal aspect of the 1st and 2nd metacarpals is unique to the radial nerve

### Patterns of damage

- wrist drop
- sensory loss to small area between the dorsal aspect of the 1st and 2nd metacarpals

### Axillary damage

- as above
- paralysis of triceps

The Framingham Heart Study is an example of a:

- ☐ A. Cross-sectional survey
- ☐ B. Cohort study
- ☐ C. Case-control study
- ☐ D. Randomised controlled trial
- ☐ E. Meta-analysis

Next question

## Study design

The following table highlights the main features of the main types of study:

<b>Randomised controlled trial</b>	<p>Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo)</p> <p>Practical or ethical problems may limit use</p>
<b>Cohort study</b>	<p>Observational and prospective. Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome.</p> <p>The usual outcome measure is the relative risk.</p> <p>Examples include Framingham Heart Study</p>
<b>Case-control study</b>	<p>Observational and retrospective. Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition.</p> <p>The usual outcome measure is the odds ratio.</p> <p>Inexpensive, produce quick results Useful for studying rare conditions Prone to confounding</p>
<b>Cross-sectional survey</b>	<p>Provide a 'snapshot', sometimes called prevalence studies</p> <p>Provide weak evidence of cause and effect</p>

Osteogenesis imperfecta is due to a defect in which one of the following proteins?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Fibrillin        |
| <input type="radio"/> | B. Elastin          |
| <input type="radio"/> | C. Type I collagen  |
| <input type="radio"/> | D. Type IV collagen |
| <input type="radio"/> | E. Polycystin-1     |

Next question

### Osteogenesis imperfecta

Osteogenesis imperfecta (more commonly known as brittle bone disease) is a group of disorders of collagen metabolism resulting in bone fragility and fractures. The most common, and milder, form of osteogenesis imperfecta is type 1

#### Overview

- autosomal dominant
- abnormality in type 1 collagen due to decreased synthesis of pro-alpha 1 or pro-alpha 2 collagen polypeptides

#### Features

- presents in childhood
- fractures
- blue sclera
- deafness secondary to otosclerosis

Which one of the following statements regarding odds and odds ratio is correct?

- ☐ A. Odds ratio = 1 / attributable risk
- ☐ B. Is always between 0 and 1 (when expressed as a decimal)
- ☐ C. The odds ratio approximates to relative risk if the outcome of interest is rare
- ☐ D. Odds ratios are the most commonly reported measure in cohort studies
- ☐ E. When applied to survival analysis is termed the hazard ratio

Next question

### Odds and odds ratio

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome. The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control.

Odds ratios are the usual reported measure in case-control studies. It approximates to relative risk if the outcome of interest is rare.

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The odds of achieving significant pain relief with paracetamol =  $40 / 20 = 2$

The odds of achieving significant pain relief with placebo =  $30 / 60 = 0.5$

Therefore the odds ratio =  $2 / 0.5 = 4$

In terms of the cell cycle, mitosis takes place in:

- |                       |       |
|-----------------------|-------|
| <input type="radio"/> | A. M  |
| <input type="radio"/> | B. M0 |
| <input type="radio"/> | C. G1 |
| <input type="radio"/> | D. S  |
| <input type="radio"/> | E. G2 |

Next question

### Cell cycle

M - Mitosis - cell division

G1 - Gap phase 1 - determines length of cell cycle - under influence of p53

S - DNA Synthesis

G2 - Gap phase

What is the correct formula to calculate the positive predictive value?

TP = true positive; FP = false positive; TN = true negative; FN = false negative

- ☐ A. Sensitivity / (1 - specificity)
- ☐ B. TP / (TP + FP)
- ☐ C. TN / (TN + FP)
- ☐ D. TN / (TN + FN)
- ☐ E. TP / (TP + FN)

Positive predictive value =  $TP / (TP + FP)$

### Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	$TP / (TP + FN)$	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	$TN / (TN + FP)$	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	$TP / (TP + FP)$	The chance that the patient has the condition if the diagnostic test is positive
<b>Negative predictive value</b>	$TN / (TN + FN)$	The chance that the patient does not have the condition if the diagnostic test is negative
<b>Likelihood ratio for a positive test result</b>	$\text{sensitivity} / (1 - \text{specificity})$	How much the odds of the disease increase when a test is positive
<b>Likelihood ratio for a negative test result</b>	$(1 - \text{sensitivity}) / \text{specificity}$	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

A randomised controlled trial is performed to look at a new drug to prevent hip fractures in postmenopausal women. Group A consists of 1,000 women who take the new drug whilst group B contains 1,400 women taking a placebo. The hip fracture rate in group A is 2% and in group B is 4%. What is the number needed to treat to prevent one hip fracture?

- ☐ A. 10
- ☒ B. 50
- ☐ C. 6
- ☐ D. 12
- ☐ E. 2

[Next question](#)

$$\text{NNT} = 1 / \text{Absolute Risk Reduction}$$

They key to answering this question is to ignore irrelevant data such as the number of patients in each group.

Control event rate = 4% = 0.04

Experimental event rate = 2% = 0.02

Absolute risk reduction = 0.04 - 0.02 = 0.02

Number needed to treat = 1 / 0.02 = 50

### Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by  $1/(\text{Absolute risk reduction})$  and is rounded to the next highest whole number

Experimental event rate (EER) = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate (CER) = (Number who had particular outcome with the control/ (Total number who had the control)

### Absolute risk reduction = CER-EER or EER-CER?

The absolute risk reduction (ARR) may be calculated by finding the absolute difference between the control event rate (CER) and the experimental event rate (EER). You will often find both versions of the above listed in different sources. In some ways it doesn't matter which you use as you will end up with the same answer but from a technical point of view:



- if the outcome of the study is undesirable then  $ARR = CER - EER$
- if the outcome of the study is desirable then  $ARR^* = EER - CER$

\*this may be more accurately termed absolute benefit increase, rather than absolute risk reduction

Where is the majority of iron found in the body?

<input type="radio"/>	A. Bone
<input type="radio"/>	B. Haemoglobin
<input type="radio"/>	C. Ferritin and haemosiderin
<input type="radio"/>	D. Myoglobin
<input type="radio"/>	E. Plasma iron

Next question

## Iron metabolism

### Absorption

- upper small intestine
- about 10% of dietary iron absorbed
- $\text{Fe}^{2+}$  (ferrous iron) much better absorbed than  $\text{Fe}^{3+}$  (ferric iron)
- absorption is regulated according to body's need
- increased by vitamin C, gastric acid
- decreased by proton pump inhibitors, tetracycline, gastric achlorhydria, tannin (found in tea)

### Distribution in body

- total body iron = 4g
- haemoglobin = 70%
- ferritin and haemosiderin = 25%
- myoglobin = 4%
- plasma iron = 0.1%

### Transport

- carried in plasma as  $\text{Fe}^{3+}$  bound to transferrin

### Storage

- stored as ferritin in tissues

### Excretion

- lost via intestinal tract following desquamation

You are a ST1 doctor in medicine. A 67-year-old man has been investigated for anaemia and weight loss. Endoscopy shows a gastric tumour which is confirmed as an adenocarcinoma on biopsy. On discussing the diagnosis the patient states that he has had 'a good life' and doesn't want any treatment. Clinical examination is unremarkable. He is able to retain and understand the information you give to him, including the likely curative nature of surgery. What is the most appropriate action?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Respect his wishes and book a follow-up appointment for four weeks                   |
| <input type="radio"/> | B. Arrange a CT head and check bloods to exclude cerebral metastases and hypercalcaemia |
| <input type="radio"/> | C. Arrange an appointment with a psychiatrist   |
| <input type="radio"/> | D. Detain him under the Mental Health Act   |
| <input type="radio"/> | E. Ask to speak to his wife alone to find out why he is refusing surgery                |

[Next question](#)

This question is ultimately about autonomy. By being able to understand and retain the information you give him the patient has demonstrated that he is competent to make decisions. It should be noted that the Mental Capacity Act 2005 states that *'a person is not to be treated as unable to make a decision merely because he makes an unwise decision'*.

A CT head and bloods may exclude causes that would impair judgement but would you override his decision even if you noticed evidence of a cerebral metastase? As there is no evidence that this man is suffering from a mental illness referral to a psychiatrist would be inappropriate.

By speaking to the wife alone you are risking breaching confidentiality. Detaining him under the Mental Health Act simply because you disagree with his decision is clearly wrong

A 54-year-old man is brought to the Emergency Department after being found collapsed in the street. He is known to have a history of alcoholic liver disease. Blood tests reveal the following:

Calcium	1.62 mmol/l
Albumin	33 g/l

Which one of the following is the most appropriate management of the calcium result?

- ☐ A. 10ml of 10% calcium chloride over 10 minutes
- ☐ B. 20% albumin infusion
- ☐ C. 10ml of 10% calcium gluconate over 10 minutes
- ☐ D. No action
- ☐ E. 10ml of 10% calcium chloride over 4 hours

Next question

Even after correction for the low albumin level this patient has significant hypocalcaemia which should be corrected.

### Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

#### Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)

Acute pancreatitis may also cause hypocalcaemia. Contamination of blood samples with EDTA may also give falsely low calcium levels

#### Management

- acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

Which one of the following statements regarding leukotrienes is not true?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Secreted by leukocytes         |
| <input type="radio"/> | B. Formed from arachidonic acid   |
| <input type="radio"/> | C. Attract leukocytes             |
| <input type="radio"/> | D. Cause bronchodilation          |
| <input type="radio"/> | E. Increase vascular permeability |

Next question

## Leukotrienes

### Function

- mediators of inflammation and allergic reactions
- cause bronchoconstriction, mucous production
- increase vascular permeability, attract leukocytes
- leukotriene D4 has been identified as the SRS-A (slow reacting substance of anaphylaxis)

### Production

- secreted by leukocytes
- formed from arachidonic acid by action of lipoxygenase
- it is thought that the NSAID induced bronchospasm in asthmatics is secondary to the express production of leukotrienes due to the inhibition of prostaglandin synthetase

A new antihypertensive is in phase III development. A study is designed where a margin is defined ( $-\delta$  to  $+\delta$ ) on mean blood pressure reduction. If the confidence interval of the difference between the new drug and ramipril lies within this margin then the trial can be said to have produced a positive result. What is this an example of?

- ☐ A. Non-inferiority trial
- ☐ B. Superiority trial
- ☐ C. Placebo-controlled trial
- ☐ D. Delta-controlled trial
- ☐ E. Equivalence trial

[Next question](#)

### Study design: new drugs

When a new drug is launched there are a number of options available in terms of study design. One option is a placebo controlled trial. Whilst this may provide robust evidence it may be considered unethical if established treatments are available and it also does not provide a comparison with standard treatments.

If a drug is therefore to be compared to an existing treatment a statistician will need to decide whether the trial is intended to show superiority, equivalence or non-inferiority:

- superiority: whilst this may seem the natural aim of a trial one problem is the large sample size needed to show a significant benefit over an existing treatment
- equivalence: an equivalence margin is defined ( $-\delta$  to  $+\delta$ ) on a specified outcome. If the confidence interval of the difference between the two drugs lies within the equivalence margin then the drugs may be assumed to have a similar effect
- non-inferiority: similar to equivalence trials, but only the lower confidence interval needs to lie within the equivalence margin (i.e.  $-\delta$ ). Small sample sizes are needed for these trials. Once a drug has been shown to be non-inferior large studies may be performed to show superiority

It should be remembered that drug companies may not necessarily want to show superiority over an existing product. If it can be demonstrated that their product is equivalent or even non-inferior then they may compete on price or convenience.

Which type of secondary messenger system does nitric oxide stimulate?

<input type="radio"/>	A. Cyclic GMP
<input type="radio"/>	B. Cyclic AMP
<input type="radio"/>	C. Phosphoinositide
<input type="radio"/>	D. Protein kinase
<input type="radio"/>	E. Calcium

Next question

## Second messengers

### Overview

- many different types
- allow amplification of external stimulus

### Cyclic AMP

- e.g. adrenaline, noradrenaline, glucagon, LH, FSH, TSH, calcitonin, parathyroid hormone

### Protein kinase activity

- e.g. insulin, growth hormone, prolactin, oxytocin, erythropoietin, growth factors

### Calcium and/or phosphoinositides

- e.g. ADH, GnRH, TRH

### Cyclic GMP

- e.g. ANP, nitric oxide

In the Gell and Coombs classification of hypersensitivity reactions idiopathic thrombocytopenic purpura is an example of a:

<input type="radio"/>	A. Type I reaction
<input type="radio"/>	B. Type II reaction
<input type="radio"/>	C. Type III reaction
<input type="radio"/>	D. Type IV reaction
<input type="radio"/>	E. Type V reaction

[Next question](#)

## Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

### Type I - Anaphylactic

- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

### Type II - Cell bound

- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

### Type III - Immune complex

- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

### Type IV - Delayed hypersensitivity

- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

### Type V - Stimulated hypersensitivity

- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis



Which one of the following clinical features would be least consistent with a diagnosis of severe pre-eclampsia?

<input type="radio"/>	A. Headache
<input type="radio"/>	B. Epigastric pain
<input type="radio"/>	C. Reflexes difficult to elicit
<input type="radio"/>	D. Low platelet count
<input type="radio"/>	E. Papilloedema

Next question

Severe pre-eclampsia is associated with hyperreflexia and clonus. A low platelet count may indicate the patient is developing HELLP syndrome

### Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria ( $> 0.3\text{g} / 24 \text{ hours}$ ). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

### Risk factors

- $> 40$  years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index  $> 30 \text{ kg/m}^2$
- diabetes mellitus
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

### Features of severe pre-eclampsia

- hypertension: typically  $> 170/110 \text{ mmHg}$  and proteinuria as above

- proteinuria: dipstick ++/+++
- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count  $< 100 \times 10^6/l$ , abnormal liver enzymes or HELLP syndrome

## Management

- consensus guidelines recommend treating blood pressure  $> 160/110$  mmHg although many clinicians have a lower threshold
- oral labetalol is now first-line following the 2010 NICE guidelines. Nifedipine and hydralazine may also be used
- delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario

A study measures a patients serum cholesterol before and after a new lipid-lowering therapy has been given. What type of significance test should be used to analyse the data?

<input type="radio"/>	A. Student's paired t-test
<input type="radio"/>	B. Student's unpaired t-test
<input type="radio"/>	C. Chi-squared test
<input type="radio"/>	D. Pearson's test
<input type="radio"/>	E. Spearman test

[Next question](#)

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Which one of the following reduces the secretion of renin?

<input type="radio"/>	A. Erect posture
<input type="radio"/>	B. Adrenaline
<input type="radio"/>	C. Hyponatraemia
<input type="radio"/>	D. Hypotension
<input type="radio"/>	E. Beta-blockers

Next question

## Renin

Renin is secreted by juxtaglomerular cells and hydrolyses angiotensinogen to produce angiotensin I

Factors stimulating renin secretion

- hypotension causing reduced renal perfusion
- hyponatraemia
- sympathetic nerve stimulation
- catecholamines
- erect posture

Factors reducing renin secretion

- drugs: beta-blockers, NSAIDs

Which one of the following is the most common underlying mechanism causing prolongation of the QT segment?

- ☐ A. Opening of calcium channels
- ☐ B. Blockage of sodium channels
- ☐ C. Opening of sodium channels
- ☐ D. Blockage of potassium channels
- ☐ E. Opening of potassium channels

Next question

Long QT syndrome - usually due to loss-of-function/blockage of K<sup>+</sup> channels

In long QT syndrome QT prolongation is due to overload of myocardial cells with positively charged ions during ventricular repolarisation. Around 90-95% of inherited causes are due to defects in potassium channels

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"> <li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li> <li>Romano-Ward syndrome (no deafness)</li> </ul>	<ul style="list-style-type: none"> <li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li> <li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li> <li>methadone</li> <li>chloroquine</li> <li>terfenadine**</li> <li>erythromycin</li> </ul>	<ul style="list-style-type: none"> <li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li> <li>acute myocardial infarction</li> <li>myocarditis</li> <li>hypothermia</li> <li>subarachnoid haemorrhage</li> </ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli

- Long QT3 - events often occur at night or at rest
- sudden cardiac death

## Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

Which of the following statements is true regarding autosomal recessive inheritance?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Disease is manifest in every generation  |
| <input type="radio"/> | B. There is a 25% chance of two heterozygote parents having a carrier child   |
| <input type="radio"/> | C. Conditions tend to be less severe than autosomal dominant conditions   |
| <input type="radio"/> | D. All offspring of an affected individual and a non-affected individual (i.e. not a carrier or affected) will be heterozygote carriers |
| <input type="radio"/> | E. Examples include Huntingdon's disease  |

Next question

### Autosomal recessive

In autosomal recessive inheritance

- only homozygotes are affected
- males and females are equally likely to be affected
- not manifest in every generation - may 'skip a generation'

If two heterozygote parents

- 25% chance of having an affected (homozygote) child
- 50% chance of having a carrier (heterozygote) child
- 25% chance of having an unaffected (i.e. genotypical) child

If one affected parent (i.e. homozygote for gene) and one unaffected (i.e. not a carrier or affected)

- all the children will be carriers

Autosomal recessive disorders are often metabolic in nature and are generally more life-threatening compared to autosomal dominant conditions

What chromosome abnormality is associated with Klinefelter's syndrome?

<input type="radio"/>	A. 47, XO
<input type="radio"/>	<b>B. 47, XXY</b>
<input type="radio"/>	C. 46, XXY
<input type="radio"/>	D. 47, XYY
<input type="radio"/>	E. 47, XXO

Next question

### Klinefelter's syndrome

Klinefelter's syndrome is associated with karyotype 47, XXY

#### Features

- often taller than average
- lack of secondary sexual characteristics
- small, firm testes
- infertile
- gynaecomastia - increased incidence of breast cancer
- elevated gonadotrophin levels

Diagnosis is by chromosomal analysis



A rapid urine screening test is developed to detect *Chlamydia*. A trial involving 200 men and women is performed comparing the new test to the existing NAAT techniques:

	<i>Chlamydia</i> present	<i>Chlamydia</i> absent
New test positive	20	3
New test negative	5	172

What is the negative predictive value of the new test?

- ☐ A. 172/177
- ☐ B. 20/23
- ☐ C. 172/192
- ☐ D. 172/175
- ☐ E. 20/25

Negative predictive value =  $TN / (TN + FN)$

=  $172 / (172 + 5)$

### Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	$TP / (TP + FN)$	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	$TN / (TN + FP)$	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	$TP / (TP + FP)$	The chance that the patient has the condition if the diagnostic test is positive
<b>Negative predictive value</b>	$TN / (TN + FN)$	The chance that the patient does not have the condition if the diagnostic test is negative
<b>Likelihood ratio for a positive test result</b>	$\text{sensitivity} / (1 - \text{specificity})$	How much the odds of the disease increase when a test is positive

<b>Likelihood ratio for a negative test result</b>	$(1 - \text{sensitivity}) / \text{specificity}$	How much the odds of the disease decrease when a test is negative
--	---	---

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

An 18-year-old male presents is reviewed in the endocrinology clinic due to concerns about delayed pubertal development, despite being 1.77m tall. On examination he has scant pubic hair and reduced testicular volume. The following blood results are obtained:

Testosterone	6.7 nmol/l (9 - 30)
LH	3.1 mu/l (3 - 10)
FSH	5.7 mu/l (3 - 10)

What is the most likely diagnosis?

- ☐ A. Klinefelter's syndrome
- ☐ B. Acute lymphoblastic leukaemia
- ☐ C. Testicular feminisation syndrome
- ☐ D. Primary testicular failure
- ☐ E. Kallman's syndrome

Next question

Klinefelter's - LH & FSH raised  
Kallman's - LH & FSH low-normal

The LH and FSH levels are inappropriately low-normal given the low testosterone concentration, which points towards a diagnosis of hypogonadotrophic hypogonadism. In Klinefelter's syndrome the LH and FSH levels are raised

### Kallman's syndrome

Kallman's syndrome is a recognised cause of delayed puberty secondary to hypogonadotrophic hypogonadism. It is usually inherited as an X-linked recessive trait. Kallman's syndrome is thought to be caused by failure of GnRH-secreting neurons to migrate to the hypothalamus.

The clue given in many questions is lack of smell (anosmia) in a boy with delayed puberty

### Features

- 'delayed puberty'
- hypogonadism, cryptorchidism
- anosmia
- sex hormone levels are low
- LH, FSH levels are inappropriately low/normal
- patients are typically of normal or above average height

Cleft lip/palate and visual/hearing defects are also seen in some patients

A 60-year-old man who is currently receiving chemotherapy for non-small cell lung cancer presents for review. He is currently being treated with oral calcium supplements as hypocalcaemia was detected during a recent admission. Bloods taken two days ago reveal the following:

Calcium	2.01 mmol/l
---------	-------------

Which one of the following tests may help determine why his calcium level remains low despite calcium supplementation?

- |                       |                         |
|-----------------------|-------------------------|
| <input type="radio"/> | A. Vitamin D            |
| <input type="radio"/> | B. Parathyroid hormone  |
| <input type="radio"/> | C. Phosphate            |
| <input type="radio"/> | D. Alkaline phosphatase |
| <input type="radio"/> | E. Magnesium            |

Next question

Cisplatin, often used in the management of non-small cell lung cancer, is a well known cause of magnesium deficiency. Without first correcting magnesium levels it is difficult to reverse hypocalcaemia.

Whilst measuring the parathyroid hormone level is always useful it is likely to be elevated unless the patient has coexistent hypoparathyroidism.

### Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

#### Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)

Acute pancreatitis may also cause hypocalcaemia. Contamination of blood samples with EDTA may also give falsely low calcium levels

#### Management

- acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

**Question 196 of 402**

Next

A 31-year-old woman presents for review. For the past few months she has been feeling generally tired and has not had a normal period for around 4 months. Prior to this she had a regular 30 day cycle. A pregnancy test is negative, pelvic examination is normal and routine bloods are ordered:

FBC	Normal
U&E	Normal
TFT	Normal
Follicle-stimulating hormone	41 iu/l ( < 35 iu/l)
Luteinizing hormone	33 mIU/l (< 20 mIU/l)
Oestradiol	70 pmol/l ( > 100 pmol/l)

What is the most likely diagnosis?

- ☐ A. Ovarian cancer
- ☐ B. Gonadotropin-producing pituitary adenoma
- ☐ C. Turner syndrome
- ☐ D. Premature ovarian failure
- ☐ E. Aromatase enzyme deficiency

Next question

**Premature ovarian failure**

Premature ovarian failure is defined as the onset of menopausal symptoms and elevated gonadotrophin levels before the age of 40 years.

**Causes**

- idiopathic - the most common cause
- chemotherapy
- autoimmune
- radiation

Features are similar to those of the normal climacteric but the actual presenting problem may differ

- climacteric symptoms: hot flushes, night sweats
- infertility
- secondary amenorrhoea
- raised FSH, LH levels

Which one of the following statements regarding epidemiological measures is correct?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Cross-sectional surveys can be used to estimate the prevalence of a condition in the population |
| <input type="radio"/> | B. In chronic diseases the incidence is much greater than the prevalence                           |
| <input type="radio"/> | C. Incidence = prevalence * duration of condition  |
| <input type="radio"/> | D. The prevalence is the number of new cases per population in a given time period                 |
| <input type="radio"/> | E. Pre-test probability = 1 / incidence  |

Next question

### Incidence and prevalence

These two terms are used to describe the frequency of a condition in a population.

The **incidence** is the number of new cases per population in a given time period.

For example, if condition X has caused 40 new cases over the past 12 months per 1,000 of the population the annual incidence is 0.04 or 4%.

The **prevalence** is the total number of cases per population at a particular point in time.

For example, imagine a questionnaire is sent to 2,500 adults asking them how much they weigh. If from this sample population of 500 of the adults were obese then the prevalence of obesity would be 0.2 or 20%.

### Relationship

- prevalence = incidence \* duration of condition
- in chronic diseases the prevalence is much greater than the incidence
- in acute diseases the prevalence and incidence are similar. For conditions such as the common cold the incidence may be greater than the prevalence

Which one of the following adrenoceptors causes inhibition of pre-synaptic neurotransmitter release in response to sympathetic stimulation?

<input type="radio"/>	A. Alpha-1
<input type="radio"/>	B. Alpha-2
<input type="radio"/>	C. Beta-1
<input type="radio"/>	D. Beta-2
<input type="radio"/>	E. Beta-3

[Next question](#)

### Adrenoceptors

#### Alpha-1

- vasoconstriction
- relaxation of GI smooth muscle
- salivary secretion
- hepatic glycogenolysis

#### Alpha-2

- mainly presynaptic: inhibition of transmitter release (inc NA, Ach from autonomic nerves)
- inhibits insulin
- platelet aggregation

#### Beta-1

- mainly located in the heart
- increase heart rate + force

#### Beta-2

- vasodilation
- bronchodilation
- relaxation of GI smooth muscle

#### Beta-3



- lipolysis

## Pathways

- all are G-protein coupled
- alpha-1: activate phospholipase C --> IP3 --> DAG
- alpha-2: inhibit adenylate cyclase
- beta-1: stimulate adenylate cyclase
- beta-2: stimulate adenylate cyclase
- beta-3: stimulate adenylate cyclase

A 43-year-old man is suspected of having a common peroneal nerve palsy following a fracture of his fibula. Each one of the following features may be seen in such lesions, except:

<input type="radio"/>	A. Wasting of the anterior tibial and peroneal muscles
<input type="radio"/>	B. Weakness of foot dorsiflexion
<input type="radio"/>	C. Weakness of extensor hallucis longus
<input type="radio"/>	D. Weakness of foot eversion
<input type="radio"/>	E. Sensory loss over the medial aspect of the lower limb

[Next question](#)

Sensory loss over the dorsum of the foot and the lower lateral part of the leg is seen in a common peroneal nerve palsy. The degree of wasting would of course depend on how long the nerve palsy had been present

### Common peroneal nerve lesion

The sciatic nerve divides into the tibial and common peroneal nerves. Injury often occurs at the neck of the fibula

The most characteristic feature of a common peroneal nerve lesion is foot drop

Other features include:

- weakness of foot dorsiflexion
- weakness of foot eversion
- weakness of extensor hallucis longus
- sensory loss over the dorsum of the foot and the lower lateral part of the leg
- wasting of the anterior tibial and peroneal muscles

**Question 200 of 402**

Which one of the following is involved in the translation of RNA into proteins?

- ☐ A. Golgi apparatus
- ☐ B. Rough endoplasmic reticulum
- ☐ C. Ribosome
- ☐ D. Smooth endoplasmic reticulum
- ☐ E. Lysosome

[Next question](#)

**Cell organelles**

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	Main function
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Aerobic respiration. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide
Proteasome	Along with lysosome pathway involved in degradation of large protein molecules

Which of the following is most likely to cause hypokalaemia associated with acidosis?

<input type="radio"/>	A. Cushing's syndrome
<input type="radio"/>	B. Vomiting
<input type="radio"/>	C. Conn's syndrome
<input type="radio"/>	D. Diuretics
<input type="radio"/>	E. Acetazolamide

Next question

### Hypokalaemia and acid-base balance

Potassium and hydrogen can be thought of as competitors. Hyperkalaemia tends to be associated with acidosis because as potassium levels rise fewer hydrogen ions can enter the cells

Hypokalaemia with alkalosis

- vomiting
- diuretics
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)

Hypokalaemia with acidosis

- diarrhoea
- renal tubular acidosis
- acetazolamide
- partially treated diabetic ketoacidosis

A 10-year-old boy is found to have haemophilia A following investigation for a haemoarthrosis. Which one of his relatives is most likely to have the condition?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Father           |
| <input type="radio"/> | B. Mother's brother |
| <input type="radio"/> | C. Father's sister  |
| <input type="radio"/> | D. Mother           |
| <input type="radio"/> | E. Father's brother |

[Next question](#)

X-linked recessive conditions are only seen in males which therefore excludes two of the options. As male to male transmission is not seen this means the answer is mother's brother.

### X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters.

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier.

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen.

Patients with deficiencies of which one of the following complement proteins are predisposed to Leiner disease?

<input type="radio"/>	A. C1
<input type="radio"/>	B. C2
<input type="radio"/>	C. C3
<input type="radio"/>	D. C4
<input type="radio"/>	E. C5

[Next question](#)

### Complement deficiencies

Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body. Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency

- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)

- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency

- causes recurrent bacterial infections

C5 deficiency

- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency

- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Each one of the following is an acute phase protein, except:

<input type="radio"/>	A. Haptoglobin
<input type="radio"/>	B. Alpha-1 antitrypsin
<input type="radio"/>	C. CRP
<input type="radio"/>	D. Ferritin
<input type="radio"/>	E. ESR

Next question

### Acute phase proteins

Acute phase proteins

- CRP
- procalcitonin
- ferritin
- fibrinogen
- alpha-1 antitrypsin
- caeruloplasmin
- serum amyloid A
- serum amyloid P component\*
- haptoglobin
- complement

During the acute phase response the liver decreases the production of other proteins (sometimes referred to as negative acute phase proteins). Examples include:

- albumin
- transthyretin (formerly known as prealbumin)
- transferrin
- retinol binding protein
- cortisol binding protein

\*plays a more significant role in other mammals such as mice

Which one of the following immunoglobulins are present in the lowest concentration in blood?

- ☐ A. IgA
- ☐ B. IgE
- ☐ C. IgG
- ☐ D. IgM
- ☐ E. IgD

Next question

Whilst the majority of IgA is found in secretions there is a significant quantity present in blood. IgE makes up less than 0.1% of immunoglobulins

### Immunoglobulins

The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

<b>IgG</b>	75%	Monomer	Enhance phagocytosis of bacteria and viruses, pass to fetal circulation
<b>IgA</b>	15%	Monomer/ dimer	Found in secretions, provide localized protection on mucous membranes
<b>IgM</b>	10%	Pentamer	first to be secreted, anti-A, B blood antibodies
<b>IgD</b>	1%	Monomer	Involved in activation of B cells
<b>IgE</b>	0.1%	Monomer	Involved in allergic reactions



Which one of the following enzymes is mainly responsible for breaking starch down into sugars?

- |                       |                      |
|-----------------------|----------------------|
| <input type="radio"/> | A. Amylase           |
| <input type="radio"/> | B. Sucrase           |
| <input type="radio"/> | C. Alpha-glucosidase |
| <input type="radio"/> | D. Maltase           |
| <input type="radio"/> | E. Lactase           |

Next question

Amylase: breaks starch down to sugars

### Gastrointestinal physiology: enzymes

Amylase is present in saliva and pancreatic secretions. It breaks starch down into sugar

The following brush border enzymes are involved in the breakdown of carbohydrates:

- maltase: cleaves disaccharide maltose to glucose + glucose
- sucrase: cleaves sucrose to fructose and glucose
- lactase: cleaves disaccharide lactose to glucose + galactose

Each one of the following promotes the release of endothelin, except:

<input type="radio"/>	A. Prostacyclin
<input type="radio"/>	B. ADH
<input type="radio"/>	C. Angiotensin II
<input type="radio"/>	D. Hypoxia
<input type="radio"/>	E. Mechanical shearing force

Next question

## Endothelin

Endothelin is a potent, long-acting vasoconstrictor and bronchoconstrictor. It is secreted initially as a prohormone by the vascular endothelium and later converted to ET-1 by the action of endothelin converting enzyme. It acts via interaction with a G-protein linked to phospholipase C leading to calcium release. Endothelin is thought to be important in the pathogenesis of many diseases including primary pulmonary hypertension (endothelin antagonists are now used), cardiac failure, hepatorenal syndrome and Raynaud's

Promotes release

- angiotensin II
- ADH
- hypoxia
- mechanical shearing forces

Inhibits release

- nitric oxide
- prostacyclin

Raised levels in

- MI
- heart failure
- ARF
- asthma
- primary pulmonary hypertension

Which one of the following diseases would give a positive cyanide-nitroprusside test?

<input type="radio"/>	A. Bartter's syndrome
<input type="radio"/>	B. Cryoglobulinaemia
<input type="radio"/>	C. Cystinuria
<input type="radio"/>	D. Paroxysmal nocturnal haemoglobinuria
<input type="radio"/>	E. Cystinosis

Next question

The cyanide-nitroprusside test would also be positive in homocystinuria

### Cystinuria

Cystinuria is an autosomal recessive disorder characterised by the formation of recurrent renal stones. It is due to a defect in the membrane transport of cystine, ornithine, lysine, arginine (mnemonic = COLA)

#### Genetics

- chromosome 2: SLC3A1 gene, chromosome 19: SLC7A9

#### Features

- recurrent renal stones
- are classically yellow and crystalline, appearing semi-opaque on x-ray

#### Diagnosis

- cyanide-nitroprusside test

#### Management

- hydration
- D-penicillamine
- urinary alkalinization

A 23-year-old man is referred to the ophthalmologists with visual problems which are found to be caused by a downward dislocation of the lens in his right eye. The ophthalmologist notices his marfanoid habitus and history of learning disabilities. A diagnosis of homocystinuria is suspected. What is the pathophysiology of this condition?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Deficiency of S-adenosyl-methionine       |
| <input type="radio"/> | B. Deficiency of homocysteine transsulfurase |
| <input type="radio"/> | C. Excess of cystathionine beta synthase     |
| <input type="radio"/> | D. Deficiency of cystathionine beta synthase |
| <input type="radio"/> | E. Excess of homocysteine transsulfurase     |

[Next question](#)

Interestingly, patients with Down's syndrome have an excess of cystathionine beta synthase.

### Homocystinuria

Homocystinuria is a rare autosomal recessive disease caused by deficiency of cystathionine beta synthase. This results in an accumulation of homocysteine which is then oxidized to homocystine.

#### Features

- often patients have fine, fair hair
- musculoskeletal: may be similar to Marfan's - arachnodactyly etc
- neurological patients may have learning difficulties, seizures
- ocular: downwards (inferonasal) dislocation of lens
- increased risk of arterial and venous thromboembolism
- also malar flush, livedo reticularis

Diagnosis is made by the cyanide-nitroprusside test, which is also positive in cystinuria

Treatment is vitamin B6 (pyridoxine) supplements

**Question 210 of 402**

Next

A new drug which may reduce the chance of patients with chronic kidney disease developing gout is introduced. In one study of 2,000 patients 1,200 received the new drug of which 120 patients develop gout. The remaining 800 patients received a placebo of which 200 developed gout. What is the absolute risk reduction of developing gout?

- ☐ A. 0.1
- ☐ B. 15%
- ☐ C. 120
- ☐ D. 25%
- ☐ E. 6.66

Next question

Absolute risk reduction = (Control event rate) - (Experimental event rate)

Absolute risk reduction = (Experimental event rate) - (Control event rate)

Control event rate =  $200 / 800 = 0.25$

Experimental event rate =  $120 / 1,200 = 0.1$

Absolute risk reduction =  $0.25 - 0.1 = 0.15 = 15\%$  reduction

**Numbers needed to treat and absolute risk reduction**

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by  $1/(\text{Absolute risk reduction})$  and is rounded to the next highest whole number

Experimental event rate (EER) = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate (CER) = (Number who had particular outcome with the control/ (Total number who had the control)

**Absolute risk reduction = CER-EER or EER-CER?**

The absolute risk reduction (ARR) may be calculated by finding the absolute difference between the control event rate (CER) and the experimental event rate (EER). You will often find both versions of the above listed in different sources. In some ways it doesn't matter which you use as you will end up with the same answer but from a technical point of view:

- if the outcome of the study is undesirable then  $ARR = CER - EER$
- if the outcome of the study is desirable then  $ARR^* = EER - CER$

\*this may be more accurately termed absolute benefit increase, rather than absolute risk reduction

Which one of the following statements regarding the normal distribution is correct?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Is a discrete probability distribution                       |
| <input type="radio"/> | B. 99.7% of values lie within 2 standard deviations of the mean |
| <input type="radio"/> | C. Mean = mode = median   |
| <input type="radio"/> | D. Standard deviation = mean / square root (variance)           |
| <input type="radio"/> | E. Is also referred to as the binomial distribution             |

Next question

The Normal distribution is a continuous probability distribution

### Normal distribution

The normal distribution is also known as the Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

Properties of the Normal distribution

- symmetrical i.e. Mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 \* SD) to the mean + (1.96 \* SD) is called the 95% confidence interval, i.e. If a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

Standard deviation

- the standard deviation (SD) is a measure of how much dispersion exists from the mean
- SD = square root (variance)

Which one of the following would cause a fall in the carbon monoxide transfer factor (TLCO)?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Goodpasture's syndrome       |
| <input type="radio"/> | B. Left-to-right cardiac shunts |
| <input type="radio"/> | C. Anaemia                      |
| <input type="radio"/> | D. Hyperkinetic states          |
| <input type="radio"/> | E. Exercise                     |

Next question

#### Transfer factor

- raised: asthma, haemorrhage, left-to-right shunts, polycythaemia
- low: everything else

#### Transfer factor

The transfer factor describes the rate at which a gas will diffuse from alveoli into blood. Carbon monoxide is used to test the rate of diffusion. Results may be given as the total gas transfer (TLCO) or that corrected for lung volume (transfer coefficient, KCO)

##### Causes of a raised TLCO

- asthma
- pulmonary haemorrhage (Wegener's, Goodpasture's)
- left-to-right cardiac shunts
- polycythaemia
- hyperkinetic states
- male gender, exercise

##### Causes of a lower TLCO

- pulmonary fibrosis
- pneumonia
- pulmonary emboli
- pulmonary oedema
- emphysema
- anaemia
- low cardiac output

KCO also tends to increase with age. Some conditions may cause an increased KCO with a normal or reduced TLCO

- pneumonectomy/lobectomy
- scoliosis/kyphosis
- neuromuscular weakness
- ankylosis of costovertebral joints e.g. ankylosing spondylitis



Chronic lymphocytic leukaemia is mostly due to a:

- |                                  |   |
|----------------------------------|---|
| <input type="radio"/>            | A. Polyclonal proliferation of B-cell lymphocytes         |
| <input checked="" type="radio"/> | B. Monoclonal proliferation of B-cell lymphocytes         |
| <input type="radio"/>            | C. Monoclonal proliferation of large granular lymphocytes |
| <input type="radio"/>            | D. Monoclonal proliferation of T-cell lymphocytes         |
| <input type="radio"/>            | E. Polyclonal proliferation of T-cell lymphocytes         |

Next question

CLL is caused by a monoclonal proliferation of B-cell lymphocytes

### Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) is caused by a monoclonal proliferation of well-differentiated lymphocytes which are almost always B-cells (99%)

#### Features

- often none
- constitutional: anorexia, weight loss
- bleeding, infections
- lymphadenopathy more marked than CML

#### Complications

- hypogammaglobulinaemia leading to recurrent infections
- warm autoimmune haemolytic anaemia in 10-15% of patients
- transformation to high-grade lymphoma (Richter's transformation)

#### Investigations

- blood film: smudge cells
- immunophenotyping

A new blood test which can show signs of myocardial damage within one hour of the onset of chest pain is developed. In a trial of 100 patients presenting with chest pain, 40 of the patients are later proven to have had myocardial ischaemia by conventional troponin tests. Of these patients the new test was positive in 20 cases. The new test was also positive in 20 of the remaining 60 patients later shown to have a negative troponin. What is the negative predictive value of the new test for myocardial ischaemia?

- ☐ A. 0.5
- ☐ B. 0.66
- ☐ C. 0.8
- ☐ D. Cannot calculate
- ☐ E. 0.33

The new test was negative in 20 of the patients later shown to have myocardial ischaemia (false negative) and negative in 40 patients confirmed not to have myocardial ischaemia (true negative)

Negative predictive value =  $TN / (TN + FN)$

$$= 40 / (40 + 20) = 0.66$$

### Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	$TP / (TP + FN)$	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	$TN / (TN + FP)$	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	$TP / (TP + FP)$	The chance that the patient has the condition if the diagnostic test is positive
<b>Negative predictive value</b>	$TN / (TN + FN)$	The chance that the patient does not have the condition if the diagnostic test is negative
<b>Likelihood ratio for a positive test result</b>	$\text{sensitivity} / (1 - \text{specificity})$	How much the odds of the disease increase when a test is positive
<b>Likelihood ratio for a negative test result</b>	$(1 - \text{sensitivity}) / \text{specificity}$	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

You are a ST1 doctor on a gastroenterology ward. The F2 doctor has asked you to supervise him putting in an ascitic drain for a patient with liver cirrhosis. He is keen to get it signed off for his portfolio. He has never seen one put in before but has read around the subject. What is the most appropriate action?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. You do the procedure but sign him off as you know he will do many more over the next 3 months                                       |
| <input type="radio"/> | B. Get the F2 doctor to insert the drain under your careful guidance, avoid telling the patient to prevent unnecessary anxiety         |
| <input type="radio"/> | C. Suggest it would be better if he watches you insert the drain before attempting one himself   |
| <input type="radio"/> | D. If he is confident ask him to do it so you can spend your time more efficiently on other ward jobs and sign him off                 |
| <input type="radio"/> | E. Ask the patient if he minds the F2 doctor doing the procedure and get the F2 doctor to insert the drain under your careful guidance |

Next question

It used to be said that for procedures 'see one, do one, teach one'. These days have long gone. Doctors are now expected to show proof of competency before performing procedures alone. In this scenario the F2 doctor has never seen one previously so it is not appropriate for him to insert the drain today. The best option is for him to watch you.

If you are going to let the F2 doctor insert the drain you should be honest with the patient about his lack of experience.

Signing him off without seeing him perform the procedure is a very poor option which could result in a GMC referral if found out. It also puts future patients at risk

Letting him insert the drain today without supervision is again a very poor option as it puts the patient at risk.

Which one of the following statements regarding allergy testing is incorrect?

- ☐ A. Both irritants and allergens may be tested for using skin patch testing
- ☐ B. The radioallergosorbent test determines the level of IgE to a specific allergen
- ☐ C. Skin prick testing is easy to perform and inexpensive
- ☐ D. Skin prick testing should be read after 48 hours
- ☐ E. Skin prick testing normally includes a histamine control

[Next question](#)

Skin prick testing can be read after 15-20 minutes. Skin patch testing is read after 48 hours

### Allergy tests

<b>Skin prick test</b>	<p>Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes</p> <p>Useful for food allergies and also pollen</p>
<b>Radioallergosorbent test (RAST)</b>	<p>Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive)</p> <p>Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom</p> <p>Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines</p>
<b>Skin patch testing</b>	<p>Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The patches are removed 48 hours later with the results being read by a dermatologist after a further 48 hours</p>

Which one of the following types of blood vessel is first to vasoconstrict in the presence of hypoxia?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Muscle arteries    |
| <input type="radio"/> | B. Skin arteries      |
| <input type="radio"/> | C. Hepatic arteries   |
| <input type="radio"/> | D. Renal arteries     |
| <input type="radio"/> | E. Pulmonary arteries |

Next question

Pulmonary arteries vasoconstrict in the presence of hypoxia

### Respiratory physiology: hypoxia

A fall in the partial pressure of oxygen in the blood leads to vasoconstriction of the pulmonary arteries. This allows blood to be diverted to better aerated areas of the lung and improves the efficiency of gaseous exchange

You review a 30-year-old man shortly after he is discharged from the Intensive Care Unit after being admitted with pneumococcal pneumonia. This is his second admission in 18 months with a severe pneumonia. During his first admission *Haemophilus influenzae* was grown from his sputum. He also describes having frequent episodes of sinusitis and recurrent skin abscesses. Which one of the following complement deficiencies is he most likely to be suffering from?

- |                                  |       |
|----------------------------------|-------|
| <input type="radio"/>            | A. C1 |
| <input type="radio"/>            | B. C2 |
| <input type="radio"/>            | C. C3 |
| <input checked="" type="radio"/> | D. C4 |
| <input type="radio"/>            | E. C5 |

[Next question](#)

### Complement deficiencies

Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body. Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency

- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)

- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency

- causes recurrent bacterial infections

C5 deficiency

- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency

- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Which one of the following features is least commonly seen in patients with pseudoxanthoma elasticum?

<input type="radio"/>	A. Increased risk of ischaemic heart disease
<input type="radio"/>	B. Retinitis pigmentosa
<input type="radio"/>	C. Gastrointestinal haemorrhage
<input type="radio"/>	D. Autosomal recessive inheritance
<input type="radio"/>	E. 'Plucked chicken skin' appearance

Next question

### Pseudoxanthoma elasticum

Pseudoxanthoma elasticum is an inherited condition (usually autosomal recessive\*) characterised by an abnormality in elastic fibres

#### Features

- retinal angioid streaks
- 'plucked chicken skin' appearance - small yellow papules on the neck, antecubital fossa and axillae
- cardiac: mitral valve prolapse, increased risk of ischaemic heart disease
- gastrointestinal haemorrhage

\*there are reports of autosomal dominant inheritance in a minority of cases



T-Helper cells of the Th1 subset typically secrete:

<input type="radio"/>	A. IFN-beta, IL-4, IL-8
<input type="radio"/>	B. IFN-gamma, IL-2, IL-3
<input type="radio"/>	C. IL-1, IL-6, TNF-alpha
<input type="radio"/>	D. IL-1
<input type="radio"/>	E. IL-4, IL-5, IL-6, IL-10, IL-13

Next question

### T-Helper cells

There are two major subsets of T-Helper cells:

Th1

- involved in the cell mediated response and delayed (type IV) hypersensitivity
- secrete IFN-gamma, IL-2, IL-3

Th2

- involved in mediating humoral (antibody) immunity
- e.g. stimulating production of IgE in asthma
- secrete IL-4, IL-5, IL-6, IL-10, IL-13

Which one of the following is equivalent to the pre-test probability?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Post test odds / (1 + post-test odds) |
| <input type="radio"/> | B. Pre-test odds x likelihood ratio      |
| <input type="radio"/> | C. The prevalence of a condition         |
| <input type="radio"/> | D. The incidence of a condition          |
| <input type="radio"/> | E. Post-test odds / likelihood ratio     |

[Next question](#)

The prevalence is the proportion of a population that have the condition at a point in time whilst the incidence is the rate at which new cases occur in a population during a specified time period.

### Pre- and post- test odds and probability

#### Pre-test probability

The proportion of people with the target disorder in the population at risk at a specific time (point prevalence) or time interval (period prevalence)

For example, the prevalence of rheumatoid arthritis in the UK is 1%

#### Post-test probability

The proportion of patients with that particular test result who have the target disorder

Post-test probability = post test odds / (1 + post-test odds)

#### Pre-test odds

The odds that the patient has the target disorder before the test is carried out

Pre-test odds = pre-test probability / (1 - pre-test probability)

#### Post-test odds

The odds that the patient has the target disorder after the test is carried out

Post-test odds = pre-test odds x likelihood ratio

where the likelihood ratio for a positive test result = sensitivity / (1 - specificity)

What is the main action of atrial natriuretic peptide?

<input type="radio"/>	A. Promotes renin excretion
<input type="radio"/>	B. Reduces excretion of sodium and water
<input type="radio"/>	C. Vasodilation
<input type="radio"/>	D. Promotes aldosterone excretion
<input type="radio"/>	E. Vasoconstriction

Next question

Atrial natriuretic peptide - powerful vasodilator

### Atrial natriuretic peptide

#### Basics

- secreted mainly from myocytes of right atrium and ventricle in response to increased blood volume
- secreted by both the right and left atria (right >> left)
- 28 amino acid peptide hormone, which acts via cGMP
- degraded by endopeptidases

#### Actions

- natriuretic, i.e. promotes excretion of sodium
- lowers BP
- antagonises actions of angiotensin II, aldosterone

A 28-year-old female undergoes a renal transplant for focal segmental glomerulosclerosis. Within hours of the operation the patient becomes unwell with features consistent with severe systemic inflammatory response syndrome. The patient is immediately taken back to theatre and the transplanted kidney is removed. What type of immunoglobulins are responsible for the graft rejection?

- |                       |        |
|-----------------------|--------|
| <input type="radio"/> | A. IgE |
| <input type="radio"/> | B. IgM |
| <input type="radio"/> | C. IgG |
| <input type="radio"/> | D. IgD |
| <input type="radio"/> | E. IgA |

[Next question](#)

Hyperacute graft rejection is due to pre-existent antibodies to HLA antigens and is therefore IgG mediated

### Renal transplant: HLA typing and graft failure

The human leucocyte antigen (HLA) system is the name given to the major histocompatibility complex (MHC) in humans. It is coded for on chromosome 6.

Some basic points on the HLA system

- class 1 antigens include A, B and C. Class 2 antigens include DP, DQ and DR
- when HLA matching for a renal transplant the relative importance of the HLA antigens are as follows DR > B > A

Graft survival

- 1 year = 90%, 10 years = 60% for cadaveric transplants
- 1 year = 95%, 10 years = 70% for living-donor transplants

Post-op problems

- ATN of graft
- vascular thrombosis
- urine leakage
- UTI

Hyperacute acute rejection (minutes to hours)

- due to pre-existent antibodies against donor HLA type 1 antigens (a type II hypersensitivity reaction)

- rarely seen due to HLA matching

#### Acute graft failure (< 6 months)

- usually due to mismatched HLA. Cell-mediated (cytotoxic T cells)
- other causes include cytomegalovirus infection
- may be reversible with steroids and immunosuppressants

#### Causes of chronic graft failure (> 6 months)

- both antibody and cell mediated mechanisms cause fibrosis to the transplanted kidney (chronic allograft nephropathy)
- recurrence of original renal disease (MCGN > IgA > FSGS)

You review a 24-year-old woman with a history of asthma in the Emergency Department. She has been admitted with acute shortness of breath associated with tongue tingling and an urticarial rash after eating a meal containing shellfish. Her symptoms settle with nebulised salbutamol and intravenous hydrocortisone. What is the most useful test to establish whether this episode was due to anaphylaxis?

- ☐ A. Serum tryptase
- ☐ B. Serum IgE
- ☐ C. Plasma histamine
- ☐ D. Eosinophil count
- ☐ E. C-reactive protein

Next question

Anaphylaxis - serum tryptase levels rise following an acute episode

Serum tryptase levels may remain elevated for up to 12 hours following an acute episode of anaphylaxis.

### Anaphylaxis

Anaphylaxis may be defined as a severe, life-threatening, generalised or systemic hypersensitivity reaction.

Anaphylaxis is one of the few times when you would not have time to look up the dose of a medication. The Resuscitation Council guidelines on anaphylaxis have recently been updated. Adrenaline is by far the most important drug in anaphylaxis and should be given as soon as possible. The recommended doses for adrenaline, hydrocortisone and chlorphenamine are as follows:

	Adrenaline	Hydrocortisone	Chlorphenamine
< 6 months	150 mcg (0.15ml 1 in 1,000)	25 mg	250 mcg/kg
6 months - 6 years	150 mcg (0.15ml 1 in 1,000)	50 mg	2.5 mg
6-12 years	300 mcg (0.3ml 1 in 1,000)	100 mg	5 mg
Adult and child > 12 years	500 mcg (0.5ml 1 in 1,000)	200 mg	10 mg

Adrenaline can be repeated every 5 minutes if necessary. The best site for IM injection is the anterolateral aspect of the middle third of the thigh.

Common identified causes of anaphylaxis

- food (e.g. Nuts) - the most common cause in children
- drugs
- venom (e.g. Wasp sting)

Which one of the following conditions is usually inherited in a X-linked dominant fashion?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Albinism              |
| <input type="radio"/> | B. Hurler's syndrome     |
| <input type="radio"/> | C. Ataxia telangiectasia |
| <input type="radio"/> | D. Homocystinuria        |
| <input type="radio"/> | E. Alport's syndrome     |

Next question

Alport's syndrome is inherited in a X-linked dominant fashion in around 85% of cases

### X-linked dominant

The following conditions are inherited in a X-linked dominant fashion\*:

Alport's syndrome (in around 85% of cases - 10-15% of cases are inherited in an autosomal recessive fashion with rare autosomal dominant variants existing)

Rett syndrome

Vitamin D resistant rickets

\*pseudohypoparathyroidism was previously classified as an X-linked dominant condition but has now been shown to be inherited in an autosomal dominant fashion in the majority of cases

A 6-year-old boy is referred to clinic due to recurrent renal calculi. His grandmother also had a similar problem. What is the most likely diagnosis?

<input type="radio"/>	A. Marfan's syndrome
<input type="radio"/>	B. Familial gout nephropathy
<input type="radio"/>	C. Homocystinuria
<input type="radio"/>	D. Cystinuria
<input type="radio"/>	E. Cystinosis

[Next question](#)

## Cystinuria

Cystinuria is an autosomal recessive disorder characterised by the formation of recurrent renal stones. It is due to a defect in the membrane transport of cystine, ornithine, lysine, arginine (mnemonic = COLA)

### Genetics

- chromosome 2: SLC3A1 gene, chromosome 19: SLC7A9

### Features

- recurrent renal stones
- are classically yellow and crystalline, appearing semi-opaque on x-ray

### Diagnosis

- cyanide-nitroprusside test

### Management

- hydration
- D-penicillamine
- urinary alkalinization



A follow-up study is performed looking at the height of 100 adults who were given steroids during childhood. The average height of the adults is 169cm, with a standard deviation of 16cm. What is the standard error of the mean?

- |                                  |                         |
|----------------------------------|-------------------------|
| <input type="radio"/>            | A. Cannot be calculated |
| <input type="radio"/>            | B. 1.69                 |
| <input type="radio"/>            | C. 0.16                 |
| <input checked="" type="radio"/> | D. 1.6                  |
| <input type="radio"/>            | E. 1.3                  |

[Next question](#)

Standard error of the mean = standard deviation / square root (number of patients)

The standard error of the mean is calculated by the standard deviation / square root (number of patients)

$$= 16 / \text{square root } (100) = 16 / 10 = 1.6$$

### Standard error of the mean

The standard error of the mean (SEM) is a measure of the spread expected for the mean of the observations - i.e. how 'accurate' the calculated sample mean is from the true population mean

Key point

- $SEM = SD / \text{square root } (n)$
- where SD = standard deviation and n = sample size

Therefore the SEM gets smaller as the sample size (n) increases

A confidence interval for the mean can be calculated in a similar way to that for a single observation, i.e. The 95% confidence interval:

- lower limit = mean - (1.96 \* SEM)
- upper limit = mean + (1.96 \* SEM)

You are a ST1 doctor working on the medical admissions unit. You are currently working for a locum consultant with whom you have a good working relationship. However, both you and the nurses are concerned regarding the some of the management decisions and inappropriate discharges. What is the most appropriate action?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Speak to the locum consultant directly  |
| <input type="radio"/> | B. Phone the local newspaper to help publicise the problem                               |
| <input type="radio"/> | C. Ask the nurses to put all the poorly or complex patients under a different consultant |
| <input type="radio"/> | D. Fill in a clinical incident form each time you disagree with a decision               |
| <input type="radio"/> | E. Speak to the medical director   |

Next question

Concerns about the performance of a more senior colleague are difficult to handle. The most important thing is not to ignore the situation. One of the advantages of speaking to the medical director is that he/she may already have concerns regarding their performance. Your comments may provide further 'evidence' on which action may be taken.

Speaking directly to the locum consultant is a possibility. He may take the attitude that given the concerns of both the medical and nursing staff it is appropriate to discuss his performance with his colleagues. It is however possible that he could become very defensive and try to stonewall you. Filling a clinical incident form would hopefully trigger management to take action but it would take time before any action or decisions are made.

Asking the nurses to put all the poorly or complex patients under a different consultant may seem attractive as it may minimise harm but it does not tackle the underlying problem and puts other patients potentially at risk from an underperforming doctor.

Phoning the local newspaper is unprofessional, unlikely to result in a speedy resolution and will uniformly decrease local confidence in the department.

Which one of the following features is characteristic of acute intermittent porphyria?

<input type="radio"/>	A. Photosensitivity
<input type="radio"/>	B. Increased urinary porphobilinogen between acute attacks
<input type="radio"/>	C. Hypernatraemia during attacks
<input type="radio"/>	D. Autosomal recessive inheritance
<input type="radio"/>	E. Increased faecal protoporphyrin excretion

Next question

### Acute intermittent porphyria

Acute intermittent porphyria (AIP) is a rare autosomal dominant condition caused by a defect in porphobilinogen deaminase, an enzyme involved in the biosynthesis of haem. The results in the toxic accumulation of delta aminolaevulinic acid and porphobilinogen. It characteristically presents with abdominal and neuropsychiatric symptoms in 20-40 year olds. AIP is more common in females (5:1)

#### Features

- abdominal: abdominal pain, vomiting
- neurological: motor neuropathy
- psychiatric: e.g. depression
- hypertension and tachycardia common

#### Diagnosis

- classically urine turns deep red on standing
- raised urinary porphobilinogen (elevated between attacks and to a greater extent during acute attacks)
- assay of red cells for porphobilinogen deaminase
- raised serum levels of delta aminolaevulinic acid and porphobilinogen

A man with glucose-6-phosphate dehydrogenase deficiency asks for advice regarding his son. What is the chance his son will also develop the disease?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. 2 in 3                      |
| <input type="radio"/> | B. No increased risk           |
| <input type="radio"/> | C. Will definitely be affected |
| <input type="radio"/> | D. 1 in 2                      |
| <input type="radio"/> | E. 1 in 4                      |

[Next question](#)

X-linked recessive conditions - no male-to-male transmission

### X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters.

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier.

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen.

A study is designed to see whether the degree of chest pain is linked to the troponin I value for patients admitted following a myocardial infarction. The pain is assessed using a scale of 1-10, with 10 representing the worst pain that the patient has ever experienced. Which one of the following significance tests is it most appropriate to use to investigate this link?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Student's t-test                        |
| <input type="radio"/> | B. Chi-squared test                        |
| <input type="radio"/> | C. Spearman's rank correlation coefficient |
| <input type="radio"/> | D. Pearson's product-moment coefficient    |
| <input type="radio"/> | E. Mann-Whitney test                       |

[Next question](#)

This scenario looks at whether the values are correlated. As the data is non-parametric, particularly the observation based pain scale, Spearman's rank correlation coefficient should be used.

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Which one of the following types of oral steroid has the least amount of mineralocorticoid activity?

- ☐ A. Fludrocortisone
- ☐ B. Hydrocortisone
- ☐ C. Dexamethasone
- ☐ D. Prednisolone
- ☐ E. Cortisone

Next question

This is clinically relevant as there are some situations where it is important to combine high glucocorticoid (anti-inflammatory) activity with minimal mineralocorticoid (fluid-retention) effects. A good example is the use of dexamethasone for patients with raised intracranial pressure secondary to brain tumours.

### Corticosteroids

Corticosteroids are amongst the most commonly prescribed therapies in clinical practice. They are used both systemically (oral or intravenous) or locally (skin creams, inhalers, eye drops, intra-articular). They augment and in some cases replace the natural glucocorticoid and mineralocorticoid activity of endogenous steroids.

The relative glucocorticoid and mineralocorticoid activity of commonly used steroids is shown below:

Minimal glucocorticoid activity, very high mineralocorticoid activity,	Glucocorticoid activity, high mineralocorticoid activity,	Predominant glucocorticoid activity, low mineralocorticoid activity	Very high glucocorticoid activity, minimal mineralocorticoid activity
Fludrocortisone	Hydrocortisone	Prednisolone	Dexamethasone Betmethasone

### Side-effects

The side-effects of corticosteroids are numerous and represent the single greatest limitation on their usage. Side-effects are more common with systemic and prolonged therapy.

#### Glucocorticoid side-effects

- endocrine: impaired glucose regulation, increased appetite/weight gain, hirsutism, hyperlipidaemia
- Cushing's syndrome: moon face, buffalo hump, striae
- musculoskeletal: osteoporosis, proximal myopathy, avascular necrosis of the femoral head
- immunosuppression: increased susceptibility to severe infection, reactivation of tuberculosis
- psychiatric: insomnia, mania, depression
- gastrointestinal: peptic ulceration, acute pancreatitis
- ophthalmic: glaucoma, cataracts
- suppression of growth in children

## Mineralocorticoid side-effects

- fluid retention
- hypertension

## Selected points on the use of corticosteroids:

- patients on long-term steroids should have their doses doubled during intercurrent illness
- the BNF suggests gradual withdrawal of systemic corticosteroids if patients have: received more than 40mg prednisolone daily for more than one week, received more than 3 weeks treatment or recently received repeated courses

What chemical mediator is mainly responsible for the tissue oedema seen in patients in hereditary angioedema?

<input type="radio"/>	A. Histamine
<input type="radio"/>	B. Serotonin
<input type="radio"/>	C. Neurokinin A
<input checked="" type="radio"/>	D. Bradykinin
<input type="radio"/>	E. Nitric oxide

[Next question](#)

### Hereditary angioedema

Hereditary angioedema is an autosomal dominant condition associated with low plasma levels of the C1 inhibitor (C1-INH) protein. C1-INH is a multifunctional serine protease inhibitor - the probable mechanism behind attacks is uncontrolled release of bradykinin resulting in oedema of tissues.

#### Investigation

- C1-INH level is low during an attack
- low C2 and C4 levels are seen, even between attacks. Serum C4 is the most reliable and widely used screening tool

#### Symptoms

- attacks may be preceded by painful macular rash
- painless, non-pruritic swelling of subcutaneous/submucosal tissues
- may affect upper airways, skin or abdominal organs (can occasionally present as abdominal pain due to visceral oedema)
- urticaria is not usually a feature

#### Management

- acute: IV C1-inhibitor concentrate, fresh frozen plasma (FFP) if this is not available
- prophylaxis: anabolic steroid Danazol may help



Each one of the following is associated with Noonan's syndrome, except:

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Webbed neck              |
| <input type="radio"/> | B. Short stature            |
| <input type="radio"/> | C. Factor XI deficiency     |
| <input type="radio"/> | D. Pulmonary valve stenosis |
| <input type="radio"/> | E. Abnormal karyotype       |

Next question

In contrast to Turner's syndrome, the karyotype is normal

### Noonan's syndrome

Often thought of as the 'male Turner's', Noonan's syndrome is an autosomal dominant condition associated with a normal karyotype. It is thought to be caused by a defect in a gene on chromosome 12

As well as features similar to Turner's syndrome (webbed neck, widely-spaced nipples, short stature, pectus carinatum and excavatum), a number of characteristic clinical signs may also be seen:

- cardiac: pulmonary valve stenosis
- ptosis
- triangular-shaped face
- low-set ears
- coagulation problems: factor XI deficiency

What is the most common target of pANCA?

<input type="radio"/>	A. Plasminogen activator inhibitor-1
<input type="radio"/>	B. Elastase
<input type="radio"/>	C. Myeloperoxidase
<input type="radio"/>	D. Serine proteinase 3
<input type="radio"/>	E. Cathepsin G

Myeloperoxidase is a neutrophil protein whose primary role is the generation of oxygen free radicals.

## ANCA

There are two main types of anti-neutrophil cytoplasmic antibodies (ANCA) - cytoplasmic (cANCA) and perinuclear (pANCA)

For the exam, remember:

- cANCA - Wegener's granulomatosis
- pANCA - Churg-Strauss syndrome + others (see below)

### cANCA

- most common target serine proteinase 3 (PR3)
- some correlation between cANCA levels and disease activity
- Wegener's granulomatosis, positive in > 90%
- microscopic polyangiitis, positive in 40%

### pANCA

- most common target is myeloperoxidase (MPO)
- cannot use level of pANCA to monitor disease activity
- associated with immune crescentic glomerulonephritis (positive in c. 80% of patients)
- microscopic polyangiitis, positive in 50-75%
- Churg-Strauss syndrome, positive in 60%
- primary sclerosing cholangitis, positive in 60-80%
- Wegener's granulomatosis, positive in 25%

Other causes of positive ANCA (usually pANCA)

- inflammatory bowel disease (UC > Crohn's)
- connective tissue disorders: RA, SLE, Sjogren's
- autoimmune hepatitis

A patient presents with an inability to abduct his right shoulder. Which nerve supplies the deltoid muscle?

- |                                  |                      |
|----------------------------------|----------------------|
| <input type="radio"/>            | A. Lateral cutaneous |
| <input type="radio"/>            | B. Suprascapular     |
| <input type="radio"/>            | C. Musculocutaneous  |
| <input checked="" type="radio"/> | D. Axillary          |
| <input type="radio"/>            | E. Median            |

[Next question](#)

Shoulder abduction - deltoid muscle - axillary nerve (C5,C6)

### Upper limb anatomy

The information below contains selected facts which commonly appear in examinations:

#### Deltoid muscle

- supplied by the axillary nerve (C5,C6)
- actions: mainly shoulder abduction

In a normal distribution what percentage of values lie within 3 standard deviations of the mean?

- |                                  |          |
|----------------------------------|----------|
| <input type="radio"/>            | A. 68.3% |
| <input type="radio"/>            | B. 98.3% |
| <input type="radio"/>            | C. 95.4% |
| <input checked="" type="radio"/> | D. 99.7% |
| <input type="radio"/>            | E. 97.2% |

[Next question](#)

### Normal distribution

The normal distribution is also known as the Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

#### Properties of the Normal distribution

- symmetrical i.e. Mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 \* SD) to the mean + (1.96 \* SD) is called the 95% confidence interval, i.e. If a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

#### Standard deviation

- the standard deviation (SD) is a measure of how much dispersion exists from the mean
- SD = square root (variance)

A 15-year-old girl presents with abdominal pain. She is normally fit and well and currently takes a combined oral contraceptive pill. The patient is accompanied by her mother, who is known to have hereditary spherocytosis. The pain is located in the upper abdomen and is episodic in nature, but has become severe today. There has been no change to her bowel habit and no nausea or vomiting. What is the most likely diagnosis?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Inferior vena cava thrombosis |
| <input type="radio"/> | B. Acute pancreatitis            |
| <input type="radio"/> | C. Renal vein thrombosis         |
| <input type="radio"/> | D. Gastritis                     |
| <input type="radio"/> | E. Biliary colic                 |

[Next question](#)

This patient has hereditary spherocytosis resulting in chronic haemolysis and gallstone formation. An important differential in a poorly patient with hereditary spherocytosis would be splenic rupture

### Hereditary spherocytosis

#### Basics

- most common hereditary haemolytic anaemia in people of northern European descent
- autosomal dominant defect of red blood cell cytoskeleton
- the normal biconcave disc shape is replaced by a sphere-shaped red blood cell
- red blood cell survival reduced as destroyed by the spleen

#### Presentation

- failure to thrive
- jaundice, gallstones
- splenomegaly
- aplastic crisis precipitated by parvovirus infection
- degree of haemolysis variable

#### Diagnosis

- osmotic fragility test

#### Management

- folate replacement
- splenectomy

A patient receives vincristine to help treat non-Hodgkin's lymphoma. What stage in the cell cycle does vincristine act?

<input type="radio"/>	A. G1
<input type="radio"/>	B. M0
<input type="radio"/>	C. M
<input type="radio"/>	D. G2
<input type="radio"/>	E. S

[Next question](#)

Vincristine inhibits formation of microtubules and arrests mitosis

### Cell cycle

M - Mitosis - cell division

G1 - Gap phase 1 - determines length of cell cycle - under influence of p53

S - DNA Synthesis

G2 - Gap phase

A new screening test is developed for colorectal cancer. It is a blood test which detects a protein; the higher the level of the protein, the more likely a patient is to have colorectal cancer. If the cut-off for a positive test is increased, which one of the following will also be increased?

- ☐ A. The p value
- ☐ B. Specificity
- ☐ C. Likelihood ratio for a negative test result
- ☐ D. Sensitivity
- ☐ E. Negative predictive value

[Next question](#)

Increasing the cut-off of a positive test result will decrease the number of false positives and hence increase the specificity

### Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	$TP / (TP + FN)$	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	$TN / (TN + FP)$	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	$TP / (TP + FP)$	The chance that the patient has the condition if the diagnostic test is positive
<b>Negative predictive value</b>	$TN / (TN + FN)$	The chance that the patient does not have the condition if the diagnostic test is negative
<b>Likelihood ratio for a positive test result</b>	$\text{sensitivity} / (1 - \text{specificity})$	How much the odds of the disease increase when a test is positive
<b>Likelihood ratio for a negative test result</b>	$(1 - \text{sensitivity}) / \text{specificity}$	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Which one of the following is not a recognised feature of methaemoglobinaemia?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Dyspnoea   |
| <input type="radio"/> | B. 'Chocolate' cyanosis   |
| <input type="radio"/> | C. Anxiety  |
| <input type="radio"/> | D. Reduced pO <sub>2</sub> but normal oxygen saturation on pulse oximetry |
| <input type="radio"/> | E. Acidosis   |

Next question

Normal pO<sub>2</sub> but decreased oxygen saturation is characteristic of methaemoglobinaemia

### Methaemoglobinaemia

Methaemoglobinaemia describes haemoglobin which has been oxidised from Fe<sup>2+</sup> to Fe<sup>3+</sup>. This is normally regulated by NADH methaemoglobin reductase, which transfers electrons from NADH to methaemoglobin resulting in the reduction of methaemoglobin to haemoglobin. There is tissue hypoxia as Fe<sup>3+</sup> cannot bind oxygen, and hence the oxidation dissociation curve is moved to the left

#### Congenital causes

- haemoglobin chain variants: HbM, HbH
- NADH methaemoglobin reductase deficiency

#### Acquired causes

- drugs: sulphonamides, nitrates, dapsone, sodium nitroprusside, primaquine
- chemicals: aniline dyes

#### Features

- 'chocolate' cyanosis
- dyspnoea, anxiety, headache
- severe: acidosis, arrhythmias, seizures, coma
- normal pO<sub>2</sub> but decreased oxygen saturation

#### Management

- NADH - methaemoglobinaemia reductase deficiency: ascorbic acid
- IV methylene blue if acquired



A study is designed to compare the calcium levels of males and females who developed inflammatory bowel disease in childhood. Which one of the following statistical tests is it most appropriate to use?

<input type="radio"/>	A. Pearson's test
<input type="radio"/>	B. Mann-Whitney test
<input type="radio"/>	C. Chi-squared test
<input type="radio"/>	D. Student's unpaired t-test
<input type="radio"/>	E. Student's paired t-test

[Next question](#)

As the data is parametric and compares two independent sample from the same population an unpaired t-test is the most appropriate test to use

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Which one of the following is not a recognised cause of hypocalcaemia?

<input type="radio"/>	A. Hypoparathyroidism
<input type="radio"/>	B. Bendroflumethiazide
<input type="radio"/>	C. Pseudohypoparathyroidism
<input type="radio"/>	D. Acute pancreatitis
<input type="radio"/>	E. Acute rhabdomyolysis

Next question

### Hypocalcaemia: causes and management

The clinical history combined with parathyroid hormone levels will reveal the cause of hypocalcaemia in the majority of cases

#### Causes

- vitamin D deficiency (osteomalacia)
- chronic renal failure
- hypoparathyroidism (e.g. post thyroid/parathyroid surgery)
- pseudohypoparathyroidism (target cells insensitive to PTH)
- rhabdomyolysis (initial stages)
- magnesium deficiency (due to end organ PTH resistance)

Acute pancreatitis may also cause hypocalcaemia. Contamination of blood samples with EDTA may also give falsely low calcium levels

#### Management

- acute management of severe hypocalcaemia is with intravenous replacement. The preferred method is with intravenous calcium gluconate, 10ml of 10% solution over 10 minutes
- intravenous calcium chloride is more likely to cause local irritation
- ECG monitoring is recommended
- further management depends on the underlying cause

A 47-year-old man is seen in the respiratory clinic. He has been referred due to progressive shortness of breath. A CT scan showed emphysematous changes in the lungs. As he has never smoked alpha 1-antitrypsin levels were ordered and reported to be 10% of normal. What is the most likely genotype of this patient?

- |                       |         |
|-----------------------|---------|
| <input type="radio"/> | A. PiZZ |
| <input type="radio"/> | B. PiSS |
| <input type="radio"/> | C. PiMS |
| <input type="radio"/> | D. PiMM |
| <input type="radio"/> | E. PiMZ |

Next question

### Alpha-1 antitrypsin deficiency

Alpha-1 antitrypsin (A1AT) deficiency is a common inherited condition caused by a lack of a protease inhibitor (Pi) normally produced by the liver. The role of A1AT is to protect cells from enzymes such as neutrophil elastase.

#### Genetics

- located on chromosome 14
- inherited in an autosomal recessive / co-dominant fashion\*
- alleles classified by their electrophoretic mobility - M for normal, S for slow, and Z for very slow
- normal = PiMM
- homozygous PiSS (50% normal A1AT levels)
- homozygous PiZZ (10% normal A1AT levels)

#### Features

- patients who manifest disease usually have PiZZ genotype
- lungs: panacinar emphysema, most marked in lower lobes
- liver: cirrhosis and hepatocellular carcinoma in adults, cholestasis in children

#### Investigations

- A1AT concentrations

#### Management

- no smoking
- supportive: bronchodilators, physiotherapy
- intravenous alpha1-antitrypsin protein concentrates
- surgery: volume reduction surgery, lung transplantation

\*trusted sources are split on which is a more accurate description

The nitric oxide receptor is an example of a:

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Ligand-gated ion channel   |
| <input type="radio"/> | B. MAPK/ERK receptor          |
| <input type="radio"/> | C. Guanylate cyclase receptor |
| <input type="radio"/> | D. G protein-coupled receptor |
| <input type="radio"/> | E. Tyrosine kinase receptor   |

Next question

The nitric oxide receptor is a soluble, intracellular guanylate cyclase

### Nitric oxide

Previously known as endothelium derived relaxation factor, nitric oxide (NO) has emerged as a molecule which is integral to many physiological and pathological processes. It is formed from L-arginine and oxygen by nitric oxide synthetase (NOS). An inducible form of NOS has been shown to be present in macrophages. Nitric oxide has a very short half-life (seconds), being inactivated by oxygen free radicals

#### Effects

- acts on guanylate cyclase leading to raised intracellular cGMP levels and therefore decreasing  $\text{Ca}^{2+}$  levels
- vasodilation, mainly venodilation
- inhibits platelet aggregation

#### Clinical relevance

- underproduction of NO is implicated in hypertrophic pyloric stenosis
- lack of NO is thought to promote atherosclerosis
- in sepsis increased levels of NO contribute to septic shock
- organic nitrates (metabolism produces NO) is widely used to treat cardiovascular disease (e.g. angina, heart failure)
- sildenafil is thought to potentiate the action of NO on penile smooth muscle and is used in the treatment of erectile dysfunctions

Which one of the following is least associated with hypercalcaemia?

<input type="radio"/>	A. Thyrotoxicosis
<input type="radio"/>	B. Secondary hyperparathyroidism
<input type="radio"/>	C. Tertiary hyperparathyroidism
<input type="radio"/>	D. Thiazide diuretics
<input type="radio"/>	E. Primary hyperparathyroidism

Next question

### Hypercalcaemia: causes

The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

- sarcoidosis\*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, calcium containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone\*\*

\*other causes of granulomas may lead to hypercalcaemia e.g. Tuberculosis and histoplasmosis

\*\*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Which one of the following immunological changes is seen in progressive HIV infection?

<input type="radio"/>	A. Increase in IL-2 production
<input type="radio"/>	B. Increase in B2-microglobulin levels
<input type="radio"/>	C. Increased type IV hypersensitivity responses
<input type="radio"/>	D. Increased natural killer (NK) cell function
<input type="radio"/>	E. A rise in the CD4/CD8 ratio

Next question

### HIV: immunology

The following immunological changes are seen in progressive HIV:

- reduction in CD4 count
- increase B2-microglobulin
- decreased IL-2 production
- polyclonal B-cell activation
- decrease NK cell function
- reduced delayed hypersensitivity responses

Which one of the following would shift the oxygen dissociation curve to the right?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Alkalosis                    |
| <input type="radio"/> | B. HbF                          |
| <input type="radio"/> | C. Low 2,3-DPG levels           |
| <input type="radio"/> | D. High pCO <sub>2</sub> levels |
| <input type="radio"/> | E. Methaemoglobin               |

[Next question](#)

### Oxygen dissociation curve

- shifts **Left** - **Lower** oxygen delivery - **Lower** acidity, temp, 2-3 DPG - also HbF, carboxy/methaemoglobin
- shifts **Right** - **Raised** oxygen delivery - **Raised** acidity, temp, 2-3 DPG

### Oxygen dissociation curve

The oxygen dissociation curve describes the relationship between the percentage of saturated haemoglobin and partial pressure of oxygen in the blood. It is not affected by haemoglobin concentration

#### Basics

- shifts to left = for given oxygen tension there is increased saturation of Hb with oxygen i.e. decreased oxygen delivery to tissues
- shifts to right = for given oxygen tension there is reduced saturation of Hb with oxygen i.e. enhanced oxygen delivery to tissues

#### Shifts to Left = Lower oxygen delivery

- HbF, methaemoglobin, carboxyhaemoglobin
- low [H<sup>+</sup>] (alkali)
- low pCO<sub>2</sub>
- low 2,3-DPG
- low temperature

#### Shifts to Right = Raised oxygen delivery

- raised [H<sup>+</sup>] (acidic)
- raised pCO<sub>2</sub>
- raised 2,3-DPG\*
- raised temperature

\*2,3-diphosphoglycerate

### Question 249 of 402

What level of evidence does a study offer which is obtained from a meta-analysis of randomised controlled trials?

<input type="radio"/>	A. Ia
<input type="radio"/>	B. Ib
<input type="radio"/>	C. IIa
<input type="radio"/>	D. IIb
<input type="radio"/>	E. IV

[Next question](#)

### Study design: evidence and recommendations

#### Levels of evidence

- Ia - evidence from meta-analysis of randomised controlled trials
- Ib - evidence from at least one randomised controlled trial
- IIa - evidence from at least one well designed controlled trial which is not randomised
- IIb - evidence from at least one well designed experimental trial
- III - evidence from case, correlation and comparative studies
- IV - evidence from a panel of experts

#### Grading of recommendation

- Grade A - based on evidence from at least one randomised controlled trial (i.e. Ia or Ib)
- Grade B - based on evidence from non-randomised controlled trials (i.e. IIa, IIb or III)
- Grade C - based on evidence from a panel of experts (i.e. IV)



Vital capacity may be defined as:

- |                       |    |   |
|-----------------------|----|---|
| <input type="radio"/> | A. | Volume inspired or expired with each breath at rest                                 |
| <input type="radio"/> | B. | Volume of air remaining after maximal expiration                                    |
| <input type="radio"/> | C. | Maximum volume of air that can be inspired at the end of a normal tidal inspiration |
| <input type="radio"/> | D. | Maximum volume of air that can be expired at the end of a normal tidal expiration   |
| <input type="radio"/> | E. | Maximum volume of air that can be expired after a maximal inspiration               |

[Next question](#)

### Respiratory physiology: lung volumes

Tidal volume (TV)

- volume inspired or expired with each breath at rest
- 500ml in males, 350ml in females

Inspiratory reserve volume (IRV) = 2-3 L

- maximum volume of air that can be inspired at the end of a normal tidal inspiration
- inspiratory capacity = TV + IRV

Expiratory reserve volume (ERV) = 750ml

- maximum volume of air that can be expired at the end of a normal tidal expiration

Residual volume (RV) = 1.2L

- volume of air remaining after maximal expiration
- increases with age
- $RV = FRC - ERV$

Vital capacity (VC) = 5L

- maximum volume of air that can be expired after a maximal inspiration
- 4,500ml in males, 3,500 mls in females
- decreases with age
- $VC = \text{inspiratory capacity} + ERV$

Total lung capacity (TLC) is the sum of the vital capacity + residual volume

A 34-year-old man is reviewed in clinic. He has recently had his annual echocardiogram showing no change in the dilation of his aortic sinuses or mitral valve prolapse. You note he is tall with pectus excavatum and arachnodactyly. His condition is primarily due to a defect in which one of the following proteins?

<input type="radio"/>	A. Polycystin-1
<input type="radio"/>	B. Fibrillin
<input type="radio"/>	C. Type IV collagen
<input type="radio"/>	D. Type I collagen
<input type="radio"/>	E. Elastin

[Next question](#)

Although fibrillin is the primary protein affected (due to a defect in the fibrillin-1 gene) it should be noted that fibrillin is used as a substrate of elastin

### Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 people.

#### Features

- tall stature with arm span to height ratio  $> 1.05$
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of  $> 20$  degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.

Which one of the following causes of hyponatraemia is least associated with a urinary sodium > 20 mmol/L?

<input type="radio"/>	A. Diuretics
<input type="radio"/>	B. Addison's
<input type="radio"/>	C. Psychogenic polydipsia
<input type="radio"/>	D. Syndrome of inappropriate ADH
<input type="radio"/>	E. Hypothyroidism

[Next question](#)

## Hyponatraemia

Hyponatraemia may be caused by water excess or sodium depletion. Causes of pseudohyponatraemia include hyperlipidaemia (increase in serum volume) or a taking blood from a drip arm. Urinary sodium and osmolarity levels aid making a diagnosis

### Urinary sodium > 20 mmol/l

Sodium depletion, renal loss (patient often hypovolaemic)

- diuretics
- Addison's
- diuretic stage of renal failure

Patient often euvolaemic

- SIADH (urine osmolality > 500 mmol/kg)
- hypothyroidism

### Urinary sodium < 20 mmol/l

Sodium depletion, extra-renal loss

- diarrhoea, vomiting, sweating
- burns, adenoma of rectum

Water excess (patient often hypervolaemic and oedematous)

- secondary hyperaldosteronism: CCF, cirrhosis
- reduced GFR: renal failure
- IV dextrose, psychogenic polydipsia

Which of the following is least recognised as a cause of macroglossia?

<input type="radio"/>	A. Amyloidosis
<input type="radio"/>	B. Turner's syndrome
<input type="radio"/>	C. Duchenne muscular dystrophy
<input type="radio"/>	D. Acromegaly
<input type="radio"/>	E. Hurler syndrome

Next question

## Macroglossia

### Causes

- hypothyroidism
- acromegaly
- amyloidosis
- Duchenne muscular dystrophy
- mucopolysaccharidosis (e.g. Hurler syndrome)

Patients with Down's syndrome are now thought to have apparent macroglossia due to a combination of mid-face hypoplasia and hypotonia

Which one of the following cell organelles contains double-stranded circular DNA?

- ☐ A. Nucleus
- ☐ B. Ribosome
- ☐ C. Nucleolus
- ☐ D. Golgi apparatus
- ☐ E. Mitochondria

Next question

### Cell organelles

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	Main function
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Aerobic respiration. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide
Proteasome	Along with lysosome pathway involved in degradation of large protein molecules

A 31-year-old woman is diagnosed with familial hypercholesterolaemia. Genetic testing shows that she is heterozygous for the condition. You discuss the possibility of screening her relatives. What is the chance her brother will also be affected?

<input type="radio"/>	A. 50%
<input type="radio"/>	B. 66%
<input type="radio"/>	C. 25%
<input type="radio"/>	D. 100%
<input type="radio"/>	E. 0%

[Next question](#)

As familial hypercholesterolaemia is an autosomal dominant condition 50% of the first-degree relatives of heterozygotes will be affected. Please see the PLoS link for more details.

### Familial hypercholesterolaemia

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that is thought to affect around 1 in 500 people. It results in high levels of LDL-cholesterol which, if untreated, may cause early cardiovascular disease (CVD). FH is caused by mutations in the gene which encodes the LDL-receptor protein.

Clinical diagnosis is now based on the **Simon Broome criteria**:

- in adults total cholesterol (TC) > 7.5 mmol/l and LDL-C > 4.9 mmol/l or children TC > 6.7 mmol/l and LDL-C > 4.0 mmol/l, plus:
- for definite FH: tendon xanthoma in patients or 1st or 2nd degree relatives or DNA-based evidence of FH
- for possible FH: family history of myocardial infarction below age 50 years in 2nd degree relative, below age 60 in 1st degree relative, or a family history of raised cholesterol levels

### Management

- the use of CVD risk estimation using standard tables is not appropriate in FH as they do not accurately reflect the risk of CVD
- referral to a specialist lipid clinic is usually required
- the maximum dose of potent statins are usually required
- first-degree relatives have a 50% chance of having the disorder and should therefore be offered screening. This includes children who should be screened by the age of 10 years if there is one affected parent
- statins should be discontinued in women 3 months before conception due to the risk of congenital defects

A small study is designed to look at the link between drinking alcohol and liver cirrhosis. One hundred patients with liver cirrhosis were questioned and it was found that 80 of them drank excessive alcohol. As a control, one hundred patients without liver cirrhosis were questioned and only 20 of these patients drank excessively. What is the odds ratio of developing liver cirrhosis for people who drink excessively compared to those who do not?

- ☐ A. 2
- ☐ B. 4
- ☐ C. 0.25
- ☒ D. 16
- ☐ E. 3

[Next question](#)

The odds of a patient with liver cirrhosis having a history of excessive drinking is  $80/20 = 4$ .

The odds of a patient without liver cirrhosis having a history of excessive drinking is  $20/80 = 0.25$ .

Therefore the odds ratio =  $4 / 0.25 = 16$

### Odds and odds ratio

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome. The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control.

Odds ratios are the usual reported measure in case-control studies. It approximates to relative risk if the outcome of interest is rare.

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Achieved = 50% pain relief
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol =  $40 / 20 = 2$

The odds of achieving significant pain relief with placebo =  $30 / 60 = 0.5$

Therefore the odds ratio =  $2 / 0.5 = 4$

Cystic fibrosis is due to a defect in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Which chromosome is this gene located on?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Chromosome 3  |
| <input type="radio"/> | B. Chromosome 7  |
| <input type="radio"/> | C. Chromosome 11 |
| <input type="radio"/> | D. Chromosome 14 |
| <input type="radio"/> | E. Chromosome 15 |

[Next question](#)

### Cystic fibrosis

Cystic fibrosis (CF) is an autosomal recessive disorder causing increased viscosity of secretions (e.g. lungs and pancreas). It is due to a defect in the cystic fibrosis transmembrane conductance regulator gene (CFTR), which codes a cAMP-regulated chloride channel

In the UK 80% of CF cases are due to delta F508 on the long arm of chromosome 7. Cystic fibrosis affects 1 per 2500 births, and the carrier rate is c. 1 in 25

Organisms which may colonise CF patients

- Staph aureus
- *Pseudomonas aeruginosa*
- Burkholderia cepacia\*
- Aspergillus

\*previously known as *Pseudomonas cepacia*



A 54-year-old woman is admitted to the Emergency Department following what sounds like an episode of vasovagal syncope. Blood gases on admission show a metabolic acidosis. Blood tests are reported as follows:

Na <sup>+</sup>	143 mmol/l
K <sup>+</sup>	3.0 mmol/l
Chloride	116 mmol/l
Bicarbonate	18 mmol/l
Urea	4.0 mmol/l
Creatinine	88 µmol/l

Which one of the following is most likely to explain the metabolic acidosis?

- ☐ A. Lithium overdose
- ☐ B. Aspirin overdose
- ☐ C. Recent myocardial infarction
- ☐ D. Alcoholic ketoacidosis
- ☐ E. Ureterosigmoidostomy

Next question

The anion gap is normal,  $(143 + 3.0) - (116 + 18) = 12$  mmol/l, which is consistent with a ureterosigmoidostomy. Aspirin overdose, myocardial infarction and alcoholic ketoacidosis would cause a raised anion gap

### Metabolic acidosis

Metabolic acidosis is commonly classified according to the anion gap. This can be calculated by:  $(\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-)$ . If a question supplies the chloride level then this is often a clue that the anion gap should be calculated. The normal range = 10-18 mmol/L

Normal anion gap ( = hyperchloraemic metabolic acidosis)

- gastrointestinal bicarbonate loss: diarrhoea, ureterosigmoidostomy, fistula
- renal tubular acidosis
- drugs: e.g. acetazolamide
- ammonium chloride injection
- Addison's disease

Raised anion gap

- lactate: shock, hypoxia
- ketones: diabetic ketoacidosis, alcohol

- urate: renal failure
- acid poisoning: salicylates, methanol

Metabolic acidosis secondary to high lactate levels may be subdivided into two types:

- lactic acidosis type A: shock, hypoxia, burns
- lactic acidosis type B: metformin

Which one of the following statements regarding the normal menstrual cycle is incorrect?

- ☐ A. A number of follicles develop in the follicular phase under the influence of FSH
- ☐ B. The luteal phase is also known as the secretory phase
- ☐ C. The follicular phase follows menstruation and occurs around day 5 - 13
- ☐ D. A surge of FSH causes ovulation
- ☐ E. Progesterone levels are low in the follicular phase

Next question

LH surge causes ovulation

## Menstrual cycle

The menstrual cycle may be divided into the following phases:

	Days
<b>Menstruation</b>	1-4
<b>Follicular phase (proliferative phase)</b>	5-13
<b>Ovulation</b>	14
<b>Luteal phase (secretory phase)</b>	15-28

Further details are given in the table below

	<b>Follicular phase (proliferative phase)</b>	<b>Luteal phase (secretory phase)</b>
<b>Ovarian histology</b>	A number of follicles develop.  One follicle will become dominant around the mid-follicular phase	Corpus luteum
<b>Endometrial histology</b>	Proliferation of endometrium	Endometrium changes to secretory lining under influence of progesterone
<b>Hormones</b>	A rise in FSH results in the development of follicles which in turn secrete oestradiol  When the egg has matured, it secretes enough oestradiol to trigger the acute release of LH. This in turn leads to ovulation	Progesterone secreted by corpus luteum rises through the luteal phase.  If fertilisation does not occur the corpus luteum will degenerate and progesterone levels fall  Oestradiol levels also rise again during the luteal phase

<b>Cervical mucus</b>	<p>Following menstruation the mucus is thick and forms a plug across the external os</p> <p>Just prior to ovulation the mucus becomes clear, acellular, low viscosity. It also becomes 'stretchy' - a quality termed spinnbarkeit</p>	<p>Under the influence of progesterone it becomes thick, scant, and tacky</p>
<b>Basal body temperature</b>	<p>Falls prior to ovulation due to the influence of oestradiol</p>	<p>Rises following ovulation in response to higher progesterone levels</p>

You are advising a patient who has recently been diagnosed with chronic kidney disease stage 4 with regards to her diet. Which one of the following foods should she eat in moderation due to the high potassium content?

<input type="radio"/>	A. Tomatoes
<input type="radio"/>	B. Plums
<input type="radio"/>	C. Cranberry juice
<input type="radio"/>	D. Grapes
<input type="radio"/>	E. Green beans

[Next question](#)

## Hyperkalaemia

Plasma potassium levels are regulated by a number of factors including aldosterone, acid-base balance and insulin levels. Metabolic acidosis is associated with hyperkalaemia as hydrogen and potassium ions compete with each other for exchange with sodium ions across cell membranes and in the distal tubule. ECG changes seen in hyperkalaemia include tall-tented T waves, small P waves, widened QRS leading to a sinusoidal pattern and asystole

Causes of hyperkalaemia:

- acute renal failure
- drugs\*: potassium sparing diuretics, ACE inhibitors, angiotensin 2 receptor blockers, spironolactone, ciclosporin, heparin\*\*
- metabolic acidosis
- Addison's
- rhabdomyolysis
- massive blood transfusion

Foods that are high in potassium:

- salt substitutes (i.e. Contain potassium rather than sodium)
- bananas, oranges, kiwi fruit, avocado, spinach, tomatoes

\*beta-blockers interfere with potassium transport into cells and can potentially cause hyperkalaemia in renal failure patients - remember beta-agonists, e.g. Salbutamol, are sometimes used as emergency treatment

\*\*both unfractionated and low-molecular weight heparin can cause hyperkalaemia. This is thought to be caused by inhibition of aldosterone secretion

Interferon-alpha may be used in the management of each one of the following, except:

<input type="radio"/>	A. Metastatic renal cell cancer
<input type="radio"/>	B. Hepatitis B
<input type="radio"/>	C. Kaposi's sarcoma
<input type="radio"/>	D. Hepatitis C
<input type="radio"/>	E. Chronic granulomatous disease

Next question

## Interferon

Interferons (IFN) are cytokines released by the body in response to viral infections and neoplasia. They are classified according to cellular origin and the type of receptor they bind to. IFN-alpha and IFN-beta bind to type 1 receptors whilst IFN-gamma binds only to type 2 receptors.

### IFN-alpha

- produced by leucocytes
- antiviral action
- useful in hepatitis B & C, Kaposi's sarcoma, metastatic renal cell cancer, hairy cell leukaemia
- adverse effects include flu-like symptoms and depression

### IFN-beta

- produced by fibroblasts
- antiviral action
- reduces the frequency of exacerbations in patients with relapsing-remitting MS

### IFN-gamma

- produced by T lymphocytes & NK cells
- weaker antiviral action, more of a role in immunomodulation particularly macrophage activation
- may be useful in chronic granulomatous disease and osteopetrosis

Northern blotting is used to:

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Detect and quantify proteins |
| <input type="radio"/> | B. Amplify DNA                  |
| <input type="radio"/> | C. Detect RNA                   |
| <input type="radio"/> | D. Detect DNA                   |
| <input type="radio"/> | E. Amplify RNA                  |

Next question

#### Molecular biology techniques

- SNOW (South - **N**Orth - **W**est)
- DROP (**D**NA - **R**NA - **P**rotein)

#### Molecular biology techniques

The following table shows a very basic summary of molecular biology techniques

Southern blotting	Detects DNA
Northern blotting	Detects RNA
Western blotting	Detects and quantifies proteins

Where is secretin secreted from?

- ☐ A. I cells in upper small intestine
- ☐ B. G cells in stomach
- ☐ C. K cells in upper small intestine
- ☐ D. D cells in the pancreas
- ☐ E. S cells in upper small intestine

[Next question](#)

### Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
<b>Gastrin</b>	G cells in antrum of the stomach	Distension of stomach, vagus nerves (mediated by gastrin-releasing peptide), luminal peptides/amino acids Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
<b>CCK</b>	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
<b>Secretin</b>	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
<b>VIP</b>	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid secretion
<b>Somatostatin</b>	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production



Each one of the following is a feature of pseudohypoparathyroidism, except:

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Short fourth and fifth metacarpals  |
| <input type="radio"/> | B. Round face                          |
| <input type="radio"/> | C. Normal calcium and phosphate levels |
| <input type="radio"/> | D. Cognitive impairment                |
| <input type="radio"/> | E. Short stature                       |

Next question

### Pseudohypoparathyroidism

Pseudohypoparathyroidism is caused by target cell insensitivity to parathyroid hormone (PTH) due to a mutation in a G-protein. In type I pseudohypoparathyroidism there is a complete receptor defect whereas in type II the cell receptor is intact. Pseudohypoparathyroidism is typically inherited in an autosomal dominant fashion\*

#### Bloods

- PTH: high
- calcium: low
- phosphate: high

#### Features

- short fourth and fifth metacarpals
- short stature
- cognitive impairment
- obesity
- round face

#### Investigation

- infusion of PTH followed by measurement of urinary phosphate and cAMP measurement - this can help differentiate between type I (neither phosphate or cAMP levels rise) and II (cAMP rises but phosphate levels do not change)

\*it was previously thought to be an X-linked dominant condition

**Question 265 of 402**

Next

A 19-year-old man with a history of learning disabilities and ectopia lentis is diagnosed as having homocystinuria. Supplementation of which one of the following may help improve his condition?

<input type="radio"/>	A. Folic acid
<input type="radio"/>	B. Niacin
<input type="radio"/>	C. Pyridoxine
<input type="radio"/>	D. Vitamin B7
<input type="radio"/>	E. Thiamine

Next question

Homocystinuria - give vitamin B6 (pyridoxine)

**Homocystinuria**

Homocystinuria is a rare autosomal recessive disease caused by deficiency of cystathionine beta synthase. This results in an accumulation of homocysteine which is then oxidized to homocystine.

**Features**

- often patients have fine, fair hair
- musculoskeletal: may be similar to Marfan's - arachnodactyly etc
- neurological patients may have learning difficulties, seizures
- ocular: downwards (inferonasal) dislocation of lens
- increased risk of arterial and venous thromboembolism
- also malar flush, livedo reticularis

Diagnosis is made by the cyanide-nitroprusside test, which is also positive in cystinuria

Treatment is vitamin B6 (pyridoxine) supplements

You are asked to design a study to assess whether living near electricity pylons is a risk factor for childhood leukaemia. What is the most appropriate type of study design?

- ☐ A. Cross-over trial
- ☐ B. Cohort study
- ☐ C. Cross-sectional survey
- ☐ D. Case-control study
- ☐ E. Randomised controlled trial

[Next question](#)

As the outcome (childhood leukaemia) is relatively rare a cohort study would take an extremely long time to provide significant results

### Study design

The following table highlights the main features of the main types of study:

<b>Randomised controlled trial</b>	<p>Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo)</p> <p>Practical or ethical problems may limit use</p>
<b>Cohort study</b>	<p>Observational and prospective. Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome.</p> <p>The usual outcome measure is the relative risk.</p> <p>Examples include Framingham Heart Study</p>
<b>Case-control study</b>	<p>Observational and retrospective. Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition.</p> <p>The usual outcome measure is the odds ratio.</p> <p>Inexpensive, produce quick results Useful for studying rare conditions Prone to confounding</p>
<b>Cross-sectional survey</b>	<p>Provide a 'snapshot', sometimes called prevalence studies</p> <p>Provide weak evidence of cause and effect</p>

You are a ST1 doctor in medicine. Whilst on-call you review a 60-year-old woman who is known to have COPD. She has been admitted with an infective exacerbation and has not responded to nebulisers and intravenous aminophylline. Her most recent blood gases show a worsening respiratory acidosis. You feel that non-invasive ventilation (NIV) is needed and bleep the on-call physio. After discussing the blood gas results over the phone she says that NIV is not indicated in her opinion and refuses to set it up. What is the most appropriate action?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Phone her back in 30 minutes and exaggerate the clinical picture to persuade her to come in |
| <input type="radio"/> | B. Accept her professional opinion and reassess the situation in 30 minutes                    |
| <input type="radio"/> | C. Set-up the NIV equipment yourself to avoid any further delay                                |
| <input type="radio"/> | D. As there is a disagreement on management speak to the consultant on-call                    |
| <input type="radio"/> | E. Transfer the patient to another hospital  |

Next question

By far the best option here is to speak to the consultant on-call. The physio may be experienced in providing NIV but it is ultimately a medical decision about whether to start a treatment.

Accepting her opinion is a poor option as she has not reviewed the patient herself and is only giving an opinion on the basis of blood gases.

Setting up NIV equipment requires training. If done incorrectly it could potentially harm a patient. Transferring an acutely unwell patient simply because the physio won't come in is not appropriate. Lying about clinical information is a very poor option.

Dobutamine is an example of:

<input type="radio"/>	A. Alpha-1 agonist
<input type="radio"/>	B. Alpha-2 agonist
<input type="radio"/>	C. Beta-1 antagonist
<input type="radio"/>	D. Beta-2 antagonist
<input type="radio"/>	E. Beta-1 agonist

Next question

### Adrenoceptor agonists

Alpha-1 agonists

- phenylephrine

Alpha-2 agonists

- clonidine

Beta-1 agonists

- dobutamine

Beta-2 agonists

- salbutamol

Beta-3 agonists

- being developed, may have a role in preventing obesity (stimulation causes lipolysis)

Which one of the following best describes the Hering-Bruer reflex?

<input type="radio"/>	A. Lung distension causing slowing of the respiratory rate
<input type="radio"/>	B. Raised hydrogen ion concentration in the ECF stimulating respiration
<input type="radio"/>	C. Low pO <sub>2</sub> stimulating the carotid and aortic bodies
<input type="radio"/>	D. Lung distension causing increase of the respiratory rate
<input type="radio"/>	E. Decreased hydrogen ion concentration in the ECF stimulating respiration

Next question

## Respiratory physiology: control

### Control of respiration

- central regulatory centres
- central and peripheral chemoreceptors
- pulmonary receptors

### Central regulatory centres

- medullary respiratory centre
- apneustic centre (lower pons)
- pneumotaxic centre (upper pons)

### Central and peripheral chemoreceptors

- central: raised [H<sup>+</sup>] in ECF stimulates respiration
- peripheral: carotid + aortic bodies, respond to raised pCO<sub>2</sub> & [H<sup>+</sup>], lesser extent low pO<sub>2</sub>

### Pulmonary receptors

- stretch receptors, lung distension causes slowing of respiratory rate (Hering-Bruer reflex)
- irritant receptor, leading to bronchoconstriction
- juxtacapillary receptors, stimulated by stretching of the microvasculature

What is the most common adverse effect experienced by women taking the progestogen only pill?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Irregular vaginal bleeding |
| <input type="radio"/> | B. Acne                       |
| <input type="radio"/> | C. Mood swings                |
| <input type="radio"/> | D. Reduced libido             |
| <input type="radio"/> | E. Weight gain                |

Next question

### Progestogen only pill: advantages/disadvantages

#### Advantages

- highly effective (failure rate = 1 per 100 woman years)
- doesn't interfere with sex
- contraceptive effects reversible upon stopping
- can be used whilst breast-feeding
- can be used in situations where the combined oral contraceptive pill is contraindicated e.g. in smokers > 35 years of age and women with a history of venous thromboembolic disease

#### Disadvantages

- irregular periods: some users may not have periods whilst others may have irregular or light periods. This is the most common adverse effect
- doesn't protect against sexually transmitted infections
- increased incidence of functional ovarian cysts
- common side-effects include breast tenderness, weight gain, acne and headaches. These symptoms generally subside after the first few months

Which one of the following causes of primary immunodeficiency is due to a defect in both B-cell and T-cell function?

<input type="radio"/>	A. Di George syndrome
<input type="radio"/>	B. Chronic granulomatous disease
<input type="radio"/>	C. Bruton's congenital agammaglobulinaemia
<input type="radio"/>	D. Leukocyte adhesion deficiency
<input type="radio"/>	E. Ataxic telangiectasia

[Next question](#)

Combined B- and T-cell disorders: SCID WAS ataxic (SCID, Wiskott-Aldrich syndrome, ataxic telangiectasia)

### Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

#### Neutrophil disorders

- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

#### B-cell disorders

- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

#### T-cell disorders

- DiGeorge syndrome

#### Combined B- and T-cell disorders

- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome



Which type of secondary messenger system does adrenaline stimulate?

<input type="radio"/>	A. Calcium
<input type="radio"/>	B. Protein kinase
<input type="radio"/>	C. Phosphoinositide
<input checked="" type="radio"/>	D. Cyclic AMP
<input type="radio"/>	E. Cyclic GMP

Next question

## Second messengers

### Overview

- many different types
- allow amplification of external stimulus

### Cyclic AMP

- e.g. adrenaline, noradrenaline, glucagon, LH, FSH, TSH, calcitonin, parathyroid hormone

### Protein kinase activity

- e.g. insulin, growth hormone, prolactin, oxytocin, erythropoietin, growth factors

### Calcium and/or phosphoinositides

- e.g. ADH, GnRH, TRH

### Cyclic GMP

- e.g. ANP, nitric oxide

A patient who takes bendroflumethiazide is noted to have a potassium of 3.1 mmol/l. What is the main mechanism causing hypokalaemia in patients taking bendroflumethiazide?

- |                                  |   |
|----------------------------------|---|
| <input type="radio"/>            | A. Decreased flow rate in the nephron resulting in a decreased potassium gradient |
| <input checked="" type="radio"/> | B. Increased sodium reaching the collecting ducts                                 |
| <input type="radio"/>            | C. Inhibition of renin-angiotensin-aldosterone system secondary to hypovolaemia   |
| <input type="radio"/>            | D. Decreased sodium reaching the distal convoluted tubule                         |
| <input type="radio"/>            | E. Opening of potassium channel in proximal convoluted tubule                     |

[Next question](#)

Bendroflumethiazide - mechanism of hypokalaemia:

- increased sodium reaching the collecting ducts
- activation of the renin-angiotensin-aldosterone

Increased delivery of sodium to the collecting ducts causes the sodium-potassium exchanger to release more potassium into the urine. Another cause is activation of the renin-angiotensin-aldosterone system secondary to hypovolaemia

### Bendroflumethiazide

Bendroflumethiazide (bendrofluazide) is a thiazide diuretic which works by inhibiting sodium absorption at the beginning of the distal convoluted tubule (DCT). Potassium is lost as a result of more sodium reaching the collecting ducts. Bendroflumethiazide has a role in the treatment of mild heart failure although loop diuretics are better for reducing overload. The main use of bendroflumethiazide was in the management of hypertension but recent NICE guidelines now recommend other thiazide-like diuretics such as indapamide and chlortalidone.

Common adverse effects

- dehydration
- postural hypotension
- hyponatraemia, hypokalaemia, hypercalcaemia
- gout
- impaired glucose tolerance
- impotence

Rare adverse effects

- thrombocytopenia

- agranulocytosis
- photosensitivity rash
- pancreatitis

(An eagle eyed user noticed that this entry is very similar to the Wikipedia one. I can assure you that the material has been cut-and-pasted from passmedicine to Wikipedia, and not vice-versa! Note the English spellings of hyponatraemia etc. Check the Wikipedia 'history' page for more details.)

Each one of the following is seen in Klinefelter's syndrome, except:

<input type="radio"/>	A. Small, firm testes
<input type="radio"/>	B. Lack of secondary sexual characteristics
<input type="radio"/>	C. Infertility
<input type="radio"/>	D. Increased incidence of breast cancer
<input type="radio"/>	E. Reduced gonadotrophin levels

Next question

### Klinefelter's syndrome

Klinefelter's syndrome is associated with karyotype 47, XXY

#### Features

- often taller than average
- lack of secondary sexual characteristics
- small, firm testes
- infertile
- gynaecomastia - increased incidence of breast cancer
- elevated gonadotrophin levels

Diagnosis is by chromosomal analysis

A 69-year-old female with a history of multiple myeloma is admitted with confusion. The following results are obtained:

Na <sup>+</sup>	147 mmol/l
K <sup>+</sup>	4.7 mmol/l
Urea	14.2 mmol/l
Creatinine	102 µmol/l
Adjusted calcium	3.9 mmol/l

What is the most appropriate initial management?

- ☐ A. IV 0.45% saline
- ☐ B. IV zoledronic acid
- ☐ C. Oral prednisolone
- ☐ D. IV pamidronate
- ☐ E. IV 0.9% saline

Next question

The raised sodium is a function of dehydration and will correct once the patient is adequately rehydrated

### Hypercalcaemia: management

The initial management of hypercalcaemia is rehydration with normal saline, typically 3-4 litres/day. Following rehydration bisphosphonates may be used. They typically take 2-3 days to work with maximal effect being seen at 7 days

Other options include:

- calcitonin - quicker effect than bisphosphonates
- steroids in sarcoidosis

There is a limited role for the use of furosemide in hypercalcaemia. It may be useful in patients who cannot tolerate aggressive fluid rehydration

A 64-year-old man is having a dual chamber pacemaker inserted. The ventricular lead is to be inserted via the coronary sinus. Where does the coronary sinus drain into?

<input type="radio"/>	A. Right atrium
<input type="radio"/>	B. Left ventricle
<input type="radio"/>	C. Right ventricle
<input type="radio"/>	D. Inferior vena cava
<input type="radio"/>	E. Left atrium

[Next question](#)

## Coronary circulation

### Arterial supply of the heart

- left aortic sinus --> left coronary artery (LCA)
- right aortic sinus --> right coronary artery (RCA)
- LCA --> LAD + circumflex
- RCA --> posterior descending
- RCA supplies SA node in 60%, AV node in 90%

### Venous drainage of the heart

- coronary sinus drains into the right atrium

A 57-year-old patient with acute pulmonary oedema is admitted to the ITU department. She has no past medical history of note. A Swan-Ganz catheter is inserted to enable measurement of the pulmonary capillary wedge pressure. Which chamber of the heart does this pressure generally equate to?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. The difference between the left atrium and right ventricle |
| <input type="radio"/> | B. Left ventricle   |
| <input type="radio"/> | C. Left atrium  |
| <input type="radio"/> | D. Right ventricle  |
| <input type="radio"/> | E. Right atrium   |

[Next question](#)

### Pulmonary capillary wedge pressure

Pulmonary capillary wedge pressure (PCWP) is measured using a balloon tipped Swan-Ganz catheter which is inserted into the pulmonary artery. The pressure measured is similar to that of the left atrium (normally 6-12 mmHg).

One of the main uses of measuring the PCWP is determining whether pulmonary oedema is caused by either heart failure or acute respiratory distress syndrome.

In many modern ITU departments PCWP measurement has been replaced by non-invasive techniques.

Which one of the following is least recognised to cause a clubbed appearance of the fingers?

<input type="radio"/>	A. Graves' disease
<input type="radio"/>	B. Empyema
<input type="radio"/>	C. Cyanotic congenital heart disease
<input type="radio"/>	D. Coeliac disease
<input type="radio"/>	E. Cystic fibrosis

Next question

Whether thyroid acropachy is a true cause of clubbing is a moot point. The question asks about a 'clubbed appearance of the fingers'

### Clubbing

The causes of clubbing may be divided into cardiac, respiratory and other

#### Cardiac causes

- cyanotic congenital heart disease (Fallot's, TGA)
- bacterial endocarditis
- atrial myxoma

#### Respiratory causes

- lung cancer
- pyogenic conditions: cystic fibrosis, bronchiectasis, abscess, empyema
- tuberculosis
- asbestosis, mesothelioma
- fibrosing alveolitis

#### Other causes

- Crohn's, to a lesser extent UC
- cirrhosis, primary biliary cirrhosis
- Graves' disease (thyroid acropachy)
- rare: Whipple's disease



**Question 279 of 402**

Next

A 14-year-old girl is admitted to hospital following a ruptured ectopic pregnancy. She comes from a family of Jehovah's Witnesses. Her haemoglobin on admission is 6.9 g/dl. She consents to a blood transfusion but her mother refuses. What is the most appropriate course of action?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Advise the parents she will have to get a High Court injunction in order to stop the transfusion |
| <input type="radio"/> | B. Give the blood transfusion   |
| <input type="radio"/> | C. Transfer the patient to a hospital run by Jehovah's Witnesses                                    |
| <input type="radio"/> | D. Respect parental wishes and withhold the blood transfusion                                       |
| <input type="radio"/> | E. Ask the hospital lawyer to come in and decide upon the correct course of action                  |

Next question

The GMC gives the following guidance:

'You should encourage young people to involve their parents in making important decisions, but you should usually abide by any decision they have the capacity to make themselves'

With respect to Jehovah's witnesses:

'You should not make assumptions about the decisions that a Jehovah's Witness patient might make about treatment with blood or blood products. You should ask for and respect their views and answer their questions honestly and to the best of your ability. You may also wish to contact the hospital liaison committees established by the Watch Tower Society (the governing body of Jehovah's Witnesses) to support Jehovah's Witnesses faced with treatment decisions involving blood. These committees can advise on current Society policy regarding the acceptability or otherwise of particular blood products. They also keep details of hospitals and doctors who are experienced in 'bloodless' medical procedures.'

A blood transfusion is clearly in the patient's best interests and in the scenario described above may potentially be life-saving. Whilst a child cannot refuse treatment they are able to provide consent. Giving the blood transfusion is therefore both clinically and ethically the right course of action.

Not giving the blood transfusion not only fails to respect the patient's wishes but also causes potential harm.

The chance of a 45-year-old mother giving birth to a child with Down's syndrome is approximately:

- ☐ A. 1 in 5
- ☐ B. 1 in 10
- ☐ C. 1 in 30
- ☐ D. 1 in 100
- ☐ E. 1 in 500

Next question

Down's syndrome risk - 1/1,000 at 30 years then divide by 3 for every 5 years

### Down's syndrome: epidemiology and genetics

Risk of Down's syndrome with increasing maternal age

- risk at 30 years = 1/1000
- 35 years = 1/350
- 40 years = 1/100
- 45 years = 1/30

One way of remembering this is by starting at 1/1,000 at 30 years and then dividing the denominator by 3 (i.e. 3 times more common) for every extra 5 years of age

### Cytogenetics

Mode	% of cases	Risk of recurrence
Non-disjunction	94%	1 in 100 if under mother < 35 years
Robertsonian translocation (usually onto 14)	5%	10-15% if mother is translocation carrier 2.5% if father is translocation carrier
Mosaicism	1%	

The chance of a further child with Down's syndrome is approximately 1 in 100 if the mother is less than 35 years old. If the trisomy 21 is a result of a translocation the risk is much higher

Which one of the following statements regarding growth hormone is incorrect?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Doesn't act directly on chondrocytes or osteoblasts                       |
| <input type="radio"/> | B. Is an anabolic hormone  |
| <input type="radio"/> | C. Is responsible for changes in protein, lipid, and carbohydrate metabolism |
| <input type="radio"/> | D. Is secreted by the somatotroph cells                                      |
| <input type="radio"/> | E. Acts on a transmembrane receptor  |

Next question

Growth hormone acts both directly on tissues (e.g. stimulates division and multiplication of cartilage chondrocytes) and also indirectly following the secretion of insulin-like growth factor 1

### Growth hormone

Growth hormone (GH) is an anabolic hormone secreted by the somatotroph cells of the anterior lobe of the pituitary gland. It has actions on multiple organ systems and is important in postnatal growth and development. Growth hormone is also responsible for changes in protein, lipid, and carbohydrate metabolism

#### Mechanism of action

- acts on a transmembrane receptor for growth
- binding of GH to the receptor leads to receptor dimerization
- acts directly on tissues and also indirectly via insulin-like growth factor 1 (IGF-1), primarily secreted by the liver

#### Conditions associated with GH disorders

- excess GH: acromegaly
- GH deficiency: resulting in short stature

The atrial natriuretic peptide receptor is an example of a:

<input type="radio"/>	A. Ligand-gated ion channel
<input type="radio"/>	B. Intracellular receptor
<input type="radio"/>	C. Guanylate cyclase receptor
<input type="radio"/>	D. G protein-coupled receptor
<input type="radio"/>	E. Tyrosine kinase receptor

Next question

## Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

Ligand-gated ion channel

- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

Tyrosine kinase receptors

- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors

- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors

- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

Which one of the following cells secretes the majority of tumour necrosis factor in humans?

<input type="radio"/>	A. Neutrophils
<input type="radio"/>	B. Macrophages
<input type="radio"/>	C. Natural killer cells
<input type="radio"/>	D. Killer-T cells
<input type="radio"/>	E. Helper-T cells

Next question

### Tumour necrosis factor

Tumour necrosis factor (TNF) is a pro-inflammatory cytokine with multiple roles in the immune system

TNF is secreted mainly by macrophages and has a number of effects on the immune system, acting mainly in a paracrine fashion:

- activates macrophages and neutrophils
- acts as costimulator for T cell activation
- key mediator of bodies response to Gram negative septicaemia
- similar properties to IL-1
- anti-tumour effect (e.g. phospholipase activation)

TNF-alpha binds to both the p55 and p75 receptor. These receptors can induce apoptosis. It also cause activation of NFkB

Endothelial effects include increase expression of selectins and increased production of platelet activating factor, IL-1 and prostaglandins

TNF promotes the proliferation of fibroblasts and their production of protease and collagenase. It is thought fragments of receptors act as binding points in serum

Systemic effects include pyrexia, increased acute phase proteins and disordered metabolism leading to cachexia

TNF is important in the pathogenesis of rheumatoid arthritis - TNF blockers (e.g. infliximab, etanercept) are now licensed for treatment of severe rheumatoid

TNF blockers

- infliximab: monoclonal antibody, IV administration

- etanercept: fusion protein that mimics the inhibitory effects of naturally occurring soluble TNF receptors, subcutaneous administration
- adalimumab: monoclonal antibody, subcutaneous administration
- adverse effects of TNF blockers include reactivation of latent tuberculosis and demyelination

Infliximab is also used in active Crohn's disease unresponsive to steroids

**Question 284 of 402**

Next

A new anti-epileptic drug is trialled for children with absence seizures. There are 250 children in the control group and 150 children assigned to take the new drug. After 4 months 100 children in the control group had had a seizure compared to 15 children in the group taking the new medication. What is the relative risk reduction?

- ☐ A. 4
- ☐ B. 30%
- ☐ C. 3.33
- ☐ D. 75%
- ☐ E. 40%

Next question

$$\text{Relative risk reduction} = (\text{EER} - \text{CER}) / \text{CER}$$

Experimental event rate,  $\text{EER} = 15 / 150 = 0.1$

Control event rate,  $\text{CER} = 100 / 250 = 0.4$

Relative risk reduction =  $(\text{EER} - \text{CER}) / \text{CER} = (0.1 - 0.4) / 0.4 = -0.75$  or a 75% reduction

**Relative risk**

**Relative risk (RR)** is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER). The term relative risk ratio is sometimes used instead of relative risk.

To recap

- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Experienced significant pain relief
Paracetamol	100	60
Placebo	80	20

Experimental event rate,  $\text{EER} = 60 / 100 = 0.6$

Control event rate,  $\text{CER} = 20 / 80 = 0.25$

Therefore the relative risk ratio =  $EER / CER = 0.6 / 0.25 = 2.4$

If the risk ratio is  $> 1$  then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is  $< 1$  then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

**Relative risk reduction (RRR)** or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate

Using the above data,  $RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140\%$



**Question 285 of 402**

Next

You are a ST1 doctor in General Medicine. During an on-call you are in A&E seeing a patient who has a pneumothorax. On arriving you find the A&E ST2 doctor attempting to perform an aspiration. He appears to about to insert the needle at the wrong landmark. What is the most appropriate action?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Tell your colleagues about what happened in the mess to ensure they are aware of the doctors limitations |
| <input type="radio"/> | B. Say nothing, stay with the patient and take over when he asks for help                                   |
| <input type="radio"/> | C. Go and get the A&E consultant  |
| <input type="radio"/> | D. Say nothing at the time but fill in a clinical incident form   |
| <input type="radio"/> | E. Immediately voice your concerns and ask him to stop  |

Next question

If you have concerns regarding the management of a patient it is important to act on them. It may be that you are wrong - the ST2 doctor may actually be performing the aspiration using a recognised, safe technique. This should not however stop you voicing your concerns - failing to do so may put the patient at risk.

If you feel unable to do so you should discuss your concerns with someone who is in a position to act. Saying nothing puts the patient at potential harm. Filling in a clinical incident form after the event will not alter this.

Spreading rumours in the mess about a doctors ability is unprofessional and unlikely to lead to a resolution of the problem.

Fragile X is associated with each one of the following, except:

<input type="radio"/>	A. Small, firm testes
<input type="radio"/>	B. Mental retardation
<input type="radio"/>	C. Hypotonia
<input type="radio"/>	D. Short stature
<input type="radio"/>	E. Large low set ears

Next question

## Fragile X

Fragile X is a trinucleotide repeat disorder

Features in males

- learning difficulties
- large low set ears, long thin face, high arched palate
- macroorchidism
- hypotonia
- autism is more common
- mitral valve prolapse

Features in females (who have one fragile chromosome and one normal X chromosome) range from normal to mild

Diagnosis

- can be made antenatally by chorionic villus sampling or amniocentesis
- analysis of the number of CGG repeats using restriction endonuclease digestion and Southern blot analysis

When establishing a screening programme, which one of the following is not a key criteria as defined by Wilson and Junger?

<input type="radio"/>	A.	There should be a recognised latent or early symptomatic stage
<input type="radio"/>	B.	The condition should be an important public health problem
<input type="radio"/>	C.	The test or examination should be acceptable to the population
<input type="radio"/>	D.	There should be agreed policy on whom to treat as patients
<input type="radio"/>	E.	The condition should be potentially curable

[Next question](#)

### Screening: Wilson and Junger criteria

1. The condition should be an important public health problem
2. There should be an acceptable treatment for patients with recognised disease
3. Facilities for diagnosis and treatment should be available
4. There should be a recognised latent or early symptomatic stage
5. The natural history of the condition, including its development from latent to declared disease should be adequately understood
6. There should be a suitable test or examination
7. The test or examination should be acceptable to the population
8. There should be agreed policy on whom to treat
9. The cost of case-finding (including diagnosis and subsequent treatment of patients) should be economically balanced in relation to the possible expenditure as a whole
10. Case-finding should be a continuous process and not a 'once and for all' project

**Question 288 of 402**

Next

A 67-year-old man presents feeling 'generally unwell' and complaining of pain in his back and legs. His wife also reports that he has been slightly confused for the past two weeks. Basic blood tests are ordered:

Hb	12.1 g/dl
Platelets	$411 \times 10^9/l$
WBC	$7.6 \times 10^9/l$

Na <sup>+</sup>	143 mmol/l
K <sup>+</sup>	5.3 mmol/l
Urea	15.7 mmol/l
Creatinine	208 $\mu$ mol/l

Bilirubin	20 $\mu$ mol/l
ALP	110 u/l
ALT	55 u/l
$\gamma$ GT	67 u/l
Albumin	31 g/l
Total protein	84 g/l

Calcium	3.10 mmol/l
Phosphate	0.79 mmol/l

What is the most likely underlying diagnosis?

- ☐ **A. Multiple myeloma**
- ☐ B. Renal cancer with bony metastases
- ☐ C. Sarcoidosis
- ☐ D. Primary hyperparathyroidism
- ☐ E. Prostate cancer with bony metastases

Next question

Hypercalcaemia, renal failure, high total protein = myeloma

One of the stand out results is the high calcium level. This immediately narrows the differential diagnosis considerably. Remember the two most common causes of hypercalcaemia are malignancy and primary hyperparathyroidism. Neither of these alone would however explain the renal failure and high total protein, both common features of untreated myeloma.

### **Myeloma: features**

Multiple myeloma is a neoplasm of the bone marrow plasma cells. The peak incidence is patients aged 60-70 years.

#### Clinical features

- bone disease: bone pain, osteoporosis + pathological fractures (typically vertebral), osteolytic lesions
- lethargy
- infection
- hypercalcaemia (see below)
- renal failure
- other features: amyloidosis e.g. Macroglossia, carpal tunnel syndrome; neuropathy; hyperviscosity

#### Diagnosis is based on:

- monoclonal proteins in the serum and urine (Bence Jones proteins)
- increased plasma cells in the bone marrow
- bone lesions on the skeletal survey

#### Hypercalcaemia in myeloma

- due primarily to increased osteoclastic bone resorption caused by local cytokines released by the myeloma cells
- other contributing factors include impaired renal function, increased renal tubular calcium reabsorption and elevated PTH-rP levels

A 29-year-old man presents with a productive cough, fever and pleuritic chest pain. A chest x-ray shows lobar consolidation and a sputum culture grows *Haemophilus influenzae*. This is his fourth chest infection in the past seven months. *Streptococcus pneumoniae* has been grown from the sputum of the previous three episodes. Six-weeks following the latest infection a full blood count, urea and electrolytes, CRP and chest x-ray are all reported as normal. What is the most appropriate next investigation?

- ☐ A. Serum immunoglobulins
- ☐ B. Spirometry
- ☐ C. HIV test
- ☐ D. Colonoscopy
- ☐ E. Urinalysis

[Next question](#)

This patient has had repeated infections with encapsulated bacteria which should raise the suspicion of immunoglobulin deficiency. HIV would be suggested by infections associated with impaired cellular immunity.

### Immunoglobulins

The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

<b>IgG</b>	75%	Monomer	Enhance phagocytosis of bacteria and viruses, pass to fetal circulation
<b>IgA</b>	15%	Monomer/ dimer	Found in secretions, provide localized protection on mucous membranes
<b>IgM</b>	10%	Pentamer	first to be secreted, anti-A, B blood antibodies
<b>IgD</b>	1%	Monomer	Involved in activation of B cells
<b>IgE</b>	0.1%	Monomer	Involved in allergic reactions

Which one of the following genetic conditions is the most prevalent in a Caucasian population?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Wilson's disease    |
| <input type="radio"/> | B. Sickle cell anaemia |
| <input type="radio"/> | C. Cystic fibrosis     |
| <input type="radio"/> | D. Alpha-1 antitrypsin |
| <input type="radio"/> | E. Haemochromatosis    |

Next question

Haemochromatosis is more common than cystic fibrosis

Haemochromatosis is an autosomal recessive disorder with a carrier rate of 1 in 10 and is present in about 1 in 200-400 people. Cystic fibrosis (CF) has a carrier rate of 1 in 25 and is present in about 1 in 2,500 births. CF is often quoted as being the most common lethal inherited condition in Caucasians

### Haemochromatosis: features

Haemochromatosis is an autosomal recessive disorder of iron absorption and metabolism resulting in iron accumulation. It is caused by inheritance of mutations in the HFE gene on both copies of chromosome 6\*. It is often asymptomatic in early disease and initial symptoms often non-specific e.g. lethargy and arthralgia

#### Epidemiology

- 1 in 10 people of European descent carry a mutation genes affecting iron metabolism, mainly HFE
- prevalence in people of European descent = 1 in 200

#### Presenting features

- early symptoms include fatigue, erectile dysfunction and arthralgia (often of the hands)
- 'bronze' skin pigmentation
- diabetes mellitus
- liver: stigmata of chronic liver disease, hepatomegaly, cirrhosis, hepatocellular deposition)
- cardiac failure (2nd to dilated cardiomyopathy)
- hypogonadism (2nd to cirrhosis and pituitary dysfunction - hypogonadotrophic hypogonadism)
- arthritis (especially of the hands)

Questions have previously been asked regarding which features are reversible with treatment:

Reversible complications	Irreversible complications
<ul style="list-style-type: none"><li>• Cardiomyopathy</li><li>• Skin pigmentation</li></ul>	<ul style="list-style-type: none"><li>• Liver cirrhosis**</li><li>• Diabetes mellitus</li><li>• Hypogonadotrophic hypogonadism</li><li>• Arthropathy</li></ul>

\*there are rare cases of families with classic features of genetic haemochromatosis but no mutation in the HFE gene

\*\*whilst elevated liver function tests and hepatomegaly may be reversible, cirrhosis is not



Which one of the following best describes the Haldane effect?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Increase in pO <sub>2</sub> means CO <sub>2</sub> binds less well to Hb      |
| <input type="radio"/> | B. Increasing acidity (or pCO <sub>2</sub> ) means oxygen binds less well to Hb |
| <input type="radio"/> | C. Decreasing acidity (or pCO <sub>2</sub> ) means oxygen binds less well to Hb |
| <input type="radio"/> | D. Raised 2,3-DPG enhances oxygen delivery to the tissues                       |
| <input type="radio"/> | E. Decrease in pO <sub>2</sub> means CO <sub>2</sub> binds less well to Hb      |

Next question

## Respiratory physiology

Chloride shift

- CO<sub>2</sub> diffuses into RBCs
- CO<sub>2</sub> + H<sub>2</sub>O  $\xrightarrow{\text{carbonic anhydrase}}$  HCO<sub>3</sub><sup>-</sup> + H<sup>+</sup>
- H<sup>+</sup> combines with Hb
- HCO<sub>3</sub><sup>-</sup> diffuses out of cell, - Cl<sup>-</sup> replaces it

Bohr effect

- increasing acidity (or pCO<sub>2</sub>) means O<sub>2</sub> binds less well to Hb

Haldane effect

- increase pO<sub>2</sub> means CO<sub>2</sub> binds less well to Hb

Which one of the following processes is responsible for ketone production during diabetic ketoacidosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Glycogenolysis                                      |
| <input type="radio"/> | B. Exchange with hydrogen ions in the collecting ducts |
| <input type="radio"/> | C. Gluconeogenesis                                     |
| <input type="radio"/> | D. Decreased plasma bicarbonate levels                 |
| <input type="radio"/> | E. Lipolysis   |

Next question

The low-insulin conditions seen in diabetic ketoacidosis stimulate the process of lipolysis and the production of the ketone bodies, beta-hydroxybutyrate and acetoacetate, which can be used as metabolic fuel.

### Diabetic ketoacidosis

The most common precipitating factors of diabetic ketoacidosis (DKA) are infection, missed insulin doses and myocardial infarction

American Diabetes Association diagnostic criteria are as follows:

- blood glucose  $>13.8$  mmol/l
- pH  $< 7.30$
- serum bicarbonate  $<18$  mmol/l
- anion gap  $> 10$
- ketonaemia

### Management

- fluid replacement: most patients with DKA are deplete around 5-8 litres. Isotonic saline is used initially
- insulin: an intravenous infusion should be started at 0.1 unit/kg/hour. Once blood glucose is  $< 15$  mmol/l an infusion of 5% dextrose should be started
- correction of hypokalaemia

### Complications of DKA and its treatment

- gastric stasis
- cerebral oedema
- thromboembolism
- acute respiratory distress syndrome
- acute renal failure

What is the main advantage of non-inferiority trials when testing a new drug?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Prevents ethical dilemmas   |
| <input type="radio"/> | B. Robust results are produced                                       |
| <input type="radio"/> | C. Useful for conditions where there is no proven drug treatment     |
| <input type="radio"/> | D. Useful for conditions where there is a high placebo response rate |
| <input type="radio"/> | E. Small sample size is required                                     |

Next question

### Study design: new drugs

When a new drug is launched there are a number of options available in terms of study design. One option is a placebo controlled trial. Whilst this may provide robust evidence it may be considered unethical if established treatments are available and it also does not provide a comparison with standard treatments.

If a drug is therefore to be compared to an existing treatment a statistician will need to decide whether the trial is intended to show superiority, equivalence or non-inferiority:

- superiority: whilst this may seem the natural aim of a trial one problem is the large sample size needed to show a significant benefit over an existing treatment
- equivalence: an equivalence margin is defined ( $-\delta$  to  $+\delta$ ) on a specified outcome. If the confidence interval of the difference between the two drugs lies within the equivalence margin then the drugs may be assumed to have a similar effect
- non-inferiority: similar to equivalence trials, but only the lower confidence interval needs to lie within the equivalence margin (i.e.  $-\delta$ ). Small sample sizes are needed for these trials. Once a drug has been shown to be non-inferior large studies may be performed to show superiority

It should be remembered that drug companies may not necessarily want to show superiority over an existing product. If it can be demonstrated that their product is equivalent or even non-inferior then they may compete on price or convenience.

**Question 294 of 402**

Next

You are a ST1 doctor in general medicine. A 19-year-old female who has type 1 diabetes mellitus is admitted with her fourth episode of diabetic ketoacidosis in the past two months. You suspect she runs her sugars high to keep her weight down. She is generally non-compliant and often self-discharges after 24 hours. What is the most appropriate response?

<input type="radio"/>	<b>A.</b> Take her on a tour of the ward showing her patients with amputated legs or those on dialysis as an incentive to get better control
<input type="radio"/>	<b>B.</b> Have a chat after the ward round about why she thinks her control is so bad
<input type="radio"/>	<b>C.</b> Write a letter to her GP advising him/her of your concerns
<input type="radio"/>	<b>D.</b> Take no action as it is her decision whether she takes her medication or complies with treatment
<input type="radio"/>	<b>E.</b> Tell her she is wasting NHS resources and you do not want to see her turn up at your hospital again

Next question

Managing young diabetic patients may be frustrating but needs to be approached in an empathetic manner. Taking time to explore why her control is so bad is the best response in this scenario. The GP should hopefully have a long term relationship with the patient and may be in a position to address these problems.

Taking no action ignores the problem. Trying to scare her by showing her patients with complications is a poor option not least because it fails to respect the privacy of the other patients.

Telling her she is wasting NHS resources is uncaring and unprofessional. Telling her not to turn up at hospital again is indefensible from an ethical and medicolegal perspective.

A new blood test is developed to screen for prostate cancer. Trials have shown it has a sensitivity for detecting clinically significant prostate cancer of 80% but a specificity of 60%. What is the likelihood ratio for a positive test result?

- ☐ A. Cannot be calculated
- ☐ B. 2
- ☐ C. 4
- ☐ D. 0.8
- ☐ E. 0.2

[Next question](#)

Likelihood ratio for a positive test result = sensitivity / (1 - specificity)

Likelihood ratio for a positive test result = sensitivity / (1 - specificity)  
 = 0.8 / (1 - 0.6) = 2

### Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	TP / (TP + FN )	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	TN / (TN + FP)	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	TP / (TP + FP)	The chance that the patient has the condition if the diagnostic test is positive
<b>Negative predictive value</b>	TN / (TN + FN)	The chance that the patient does not have the condition if the diagnostic test is negative
<b>Likelihood ratio for a positive test result</b>	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive
<b>Likelihood ratio for a negative test result</b>	(1 - sensitivity) / specificity	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

What is the initial physiological response to the Valsalva manoeuvre?

<input type="radio"/>	A. Reduction in cardiac output
<input type="radio"/>	B. Reduced mean arterial blood pressure
<input type="radio"/>	C. Reduced heart rate
<input checked="" type="radio"/>	D. Reduced venous return
<input type="radio"/>	E. Reduction in intrathoracic pressure

Next question

### Valsalva manoeuvre

The Valsalva manoeuvre describes a forced expiration against a closed glottis. This leads to increased intrathoracic pressure which in turn has a number of effects on the cardiovascular system.

#### Uses

- to terminate an episode of supraventricular tachycardia
- normalizing middle-ear pressures

#### Stages of the Valsalva manoeuvre

- 1. Increased intrathoracic pressure
- 2. Resultant increase in venous and right atrial pressure reduces venous return
- 3. The reduced preload leads to a fall in the cardiac output (Frank-Starling mechanism)
- 4. When the pressure is released there is a further slight fall in cardiac output due to increased aortic volume
- 5. Return of normal cardiac output

A study is proposed to ascertain whether childhood obesity in girls increases the risk of polycystic ovarian syndrome. What is the most appropriate form of study design?

- ☐ A. Cohort study
- ☐ B. Case-control study
- ☐ C. Cross-over trial
- ☐ D. Randomised controlled trial
- ☐ E. Cross-sectional survey

[Next question](#)

A cohort study would provide more robust evidence than a case-control study.

### Study design

The following table highlights the main features of the main types of study:

<b>Randomised controlled trial</b>	<p>Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo)</p> <p>Practical or ethical problems may limit use</p>
<b>Cohort study</b>	<p>Observational and prospective. Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome.</p> <p>The usual outcome measure is the relative risk.</p> <p>Examples include Framingham Heart Study</p>
<b>Case-control study</b>	<p>Observational and retrospective. Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition.</p> <p>The usual outcome measure is the odds ratio.</p> <p>Inexpensive, produce quick results Useful for studying rare conditions Prone to confounding</p>
<b>Cross-sectional survey</b>	<p>Provide a 'snapshot', sometimes called prevalence studies</p> <p>Provide weak evidence of cause and effect</p>

Which one of the following is least likely to cause hypernatraemia?

<input type="radio"/>	A. IV saline infusion
<input type="radio"/>	B. Hyperosmolar non-ketotic diabetic coma
<input type="radio"/>	C. Digoxin therapy
<input type="radio"/>	D. Diabetes insipidus
<input type="radio"/>	E. Dehydration

Next question

## Hypernatraemia

Causes of hypernatraemia

- dehydration
- osmotic diuresis e.g. hyperosmolar non-ketotic diabetic coma
- diabetes insipidus
- excess IV saline



A 52-year-old obese lady with type 2 diabetes mellitus is interested in changing her diet. Which one of the following foods has the highest glycaemic index?

- |                       |                      |
|-----------------------|----------------------|
| <input type="radio"/> | A. Baked potato      |
| <input type="radio"/> | B. Apple             |
| <input type="radio"/> | C. Peanut            |
| <input type="radio"/> | D. Digestive biscuit |
| <input type="radio"/> | E. Brown rice        |

[Next question](#)

Whilst white rice has a glycaemic index of 87 brown rice has a much lower value of 58

### Glycaemic index

The glycaemic index (GI) describes the capacity of a food to raise blood glucose compared with glucose in normal glucose-tolerant individuals. Foods with a high GI may be associated with an increased risk of obesity and the post-prandial hyperglycaemia associated with such foods may also increase the risk of type 2 diabetes mellitus.

High GI	White rice (87), baked potato (85), white bread (70)
Medium GI	Couscous (65), boiled new potato (62), digestive biscuit (59), brown rice (58)
Low GI	Fruit and vegetables, peanuts

The glycaemic index is shown in brackets. Glucose, by definition, would have a glycaemic index of 100

Of the following scenarios, which one would indicate it was inappropriate for the patient to take an airline flight?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. A 54-year-old woman who had a laparoscopic cholecystectomy 5 days ago  |
| <input type="radio"/> | B. A 17-year-old flying back to the UK who broke his leg whilst skiing in Canada. Had a plaster cast applied 24 hours ago |
| <input type="radio"/> | C. A 59-year-old man who had a colonoscopy 2 days ago   |
| <input type="radio"/> | D. A 62-year-old man who had an uncomplicated myocardial infarction 3 weeks ago   |
| <input type="radio"/> | E. A woman who is 27-weeks pregnant with twins  |

Next question

Following the application of a plaster cast patients should wait 24 hours before short flights (< 2 hours) and 48 hours before longer flights. This is due to the fact that air may be trapped beneath the cast

### Fitness to fly

The Civil Aviation Authority (CAA) has issued guidelines on air travel for people with medical conditions; please see the link provided.

#### Cardiovascular disease

- unstable angina, uncontrolled hypertension, uncontrolled cardiac arrhythmia, decompensated heart failure, severe symptomatic valvular disease: should not fly
- uncomplicated myocardial infarction: may fly after 7-10 days
- complicated myocardial infarction: after 4-6 weeks
- coronary artery bypass graft: after 10-14 days
- percutaneous coronary intervention: after 5 days

#### Respiratory disease

- pneumonia: should be 'clinically improved with no residual infection'
- pneumothorax: absolute contraindication, the CAA suggest patients may travel 2 weeks after successful drainage if there is no residual air. The British Thoracic Society used to recommend not travelling by air for a period of 6 weeks but this has now been changed to 1 week post check x-ray

#### Pregnancy

- most airlines do not allow travel after 36 weeks for a single pregnancy and after 32 weeks for a multiple pregnancy
- most airlines require a certificate after 28 weeks confirming that the pregnancy is progressing normally

## Surgery

- travel should be avoided for 10 days following abdominal surgery
- laparoscopic surgery: after 24 hours
- colonoscopy: after 24 hours
- following the application of a plaster cast, the majority of airlines restrict flying for 24 hours on flights of less than 2 hours or 48 hours for longer flights

## Haematological disorders

- patients with a haemoglobin of greater than 8 g/dl may travel without problems (assuming there is no coexisting condition such as cardiovascular or respiratory disease)

Which one of the following statements regarding vitamin D-resistant rickets is false?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Management includes the use of high-dose vitamin D supplements |
| <input type="radio"/> | B. Is a X-linked dominant condition                               |
| <input type="radio"/> | C. X-ray changes include cupped metaphyses                        |
| <input type="radio"/> | D. Failure to thrive may be seen                                  |
| <input type="radio"/> | E. Decreased urinary phosphate is characteristic                  |

Next question

### Vitamin D-resistant rickets

Vitamin D-resistant rickets is a X-linked dominant condition which usually presents in infancy with failure to thrive. It is caused by impaired phosphate reabsorption in the renal tubules

#### Features

- failure to thrive
- normal serum calcium, low phosphate, elevated alkaline phosphatase
- x-ray changes: cupped metaphyses with widening of the epiphyses

Diagnosis is made by demonstrating increased urinary phosphate

#### Management

- high-dose vitamin D supplements
- oral phosphate supplements

Where is B-type natriuretic peptide mainly secreted from?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Atrial myocardium      |
| <input type="radio"/> | B. Juxtaglomerular cells  |
| <input type="radio"/> | C. Zona glomerulosa       |
| <input type="radio"/> | D. Ventricular myocardium |
| <input type="radio"/> | E. Hypothalamus           |

Next question

B-type natriuretic peptide is mainly secreted by the ventricular myocardium

### B-type natriuretic peptide

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain.

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

#### Effects of BNP

- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

### Clinical uses of BNP

#### Diagnosing patients with acute dyspnoea

- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis
- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure

#### Prognosis in patients with chronic heart failure

- initial evidence suggests BNP is an extremely useful marker of prognosis

Guiding treatment in patients with chronic heart failure

- effective treatment lowers BNP levels

Screening for cardiac dysfunction

- not currently recommended for population screening

What is the role of troponin in cardiac muscle?

- ☐ A. Component of the thick filaments
- ☐ B. Acts as a lining of the T tubules
- ☐ C. Anchors thick filament to Z-discs
- ☐ D. Component of the thin filaments
- ☐ E. Anchors thick and thin filaments together

[Next question](#)

The other components of thin filaments are actin and tropomyosin. Thick filaments are primarily composed of myosin.

### Cardiac enzymes and protein markers

Interpretation of the various cardiac enzymes has now largely been superseded by the introduction of troponin T and I. Questions still however commonly appear in the MRCP

Key points for the exam

- myoglobin is the first to rise
- CK-MB is useful to look for reinfarction as it returns to normal after 2-3 days (troponin T remains elevated for up to 10 days)

	Begins to rise	Peak value	Returns to normal
<b>Myoglobin</b>	1-2 hours	6-8 hours	1-2 days
<b>CK-MB</b>	2-6 hours	16-20 hours	2-3 days
<b>CK</b>	4-8 hours	16-24 hours	3-4 days
<b>Trop T</b>	4-6 hours	12-24 hours	7-10 days
<b>AST</b>	12-24 hours	36-48 hours	3-4 days
<b>LDH</b>	24-48 hours	72 hours	8-10 days

A 79-year-old complains of lower urinary tract symptoms. Which one of the following statements regarding benign prostatic hyperplasia is incorrect?

<input type="radio"/>	A. Goserelin is licensed for refractory cases
<input type="radio"/>	B. Side-effects of 5 alpha-reductase inhibitors include ejaculation disorders and gynaecomastia
<input type="radio"/>	C. Possible presentations include recurrent urinary tract infection
<input type="radio"/>	D. 5 alpha-reductase inhibitors typically decrease the prostate specific antigen level
<input type="radio"/>	E. More common in black men

Next question

Goserelin (Zoladex) is not used in the management of benign prostatic hyperplasia

### Benign prostatic hyperplasia

Benign prostatic hyperplasia (BPH) is a common condition seen in older men.

#### Risk factors

- age: around 50% of 50-year-old men will have evidence of BPH and 30% will have symptoms. Around 80% of 80-year-old men have evidence of BPH
- ethnicity: black > white > Asian

BPH typically presents with lower urinary tract symptoms (LUTS), which may be categorised into:

- voiding symptoms (obstructive): weak or intermittent urinary flow, straining, hesitancy, terminal dribbling and incomplete emptying
- storage symptoms (irritative) urgency, frequency, urgency incontinence and nocturia
- post-micturition: dribbling
- complications: urinary tract infection, retention, obstructive uropathy

#### Management options

- watchful waiting
- medication: alpha-1 antagonists, 5 alpha-reductase inhibitors. The use of combination therapy was supported by the Medical Therapy Of Prostatic Symptoms (MTOPS) trial
- surgery: transurethral resection of prostate (TURP)

Alpha-1 antagonists e.g. tamsulosin, alfuzosin



- decrease smooth muscle tone (prostate and bladder)
- considered first-line, improve symptoms in around 70% of men
- adverse effects: dizziness, postural hypotension, dry mouth, depression

#### 5 alpha-reductase inhibitors e.g. finasteride

- block the conversion of testosterone to dihydrotestosterone (DHT), which is known to induce BPH
- unlike alpha-1 antagonists causes a reduction in prostate volume and hence may slow disease progression. This however takes time and symptoms may not improve for 6 months. They may also decrease PSA concentrations by up to 50%
- adverse effects: erectile dysfunction, reduced libido, ejaculation problems, gynaecomastia

Which one of the following types of immunoglobulins are responsible for haemolytic blood transfusion reactions?

- ☐ A. IgD
- ☐ B. IgE
- ☐ C. IgM
- ☐ D. IgA
- ☐ E. IgG

Next question

### Immunoglobulins

The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

<b>IgG</b>	75%	Monomer	Enhance phagocytosis of bacteria and viruses, pass to fetal circulation
<b>IgA</b>	15%	Monomer/ dimer	Found in secretions, provide localized protection on mucous membranes
<b>IgM</b>	10%	Pentamer	first to be secreted, anti-A, B blood antibodies
<b>IgD</b>	1%	Monomer	Involved in activation of B cells
<b>IgE</b>	0.1%	Monomer	Involved in allergic reactions

You review a 29-year-old woman who is recovering from a fracture of the right olecranon. Since the fracture she has noticed that the little finger on her right hand is numb. Which nerve is likely to have been damaged?

<input type="radio"/>	A. Ulnar nerve
<input type="radio"/>	B. Radial nerve
<input type="radio"/>	C. Axillary nerve
<input type="radio"/>	D. Musculocutaneous nerve
<input type="radio"/>	E. Median nerve

[Next question](#)

## Ulnar nerve

### Overview

- arises from medial cord of brachial plexus (C8, T1)

### Motor to

- medial two lumbricals
- adductor pollicis
- interossei
- hypothenar muscles: abductor digiti minimi, flexor digiti minimi
- flexor carpi ulnaris

### Sensory to

- medial 1 1/2 fingers (palmar and dorsal aspects)

## Patterns of damage

### Damage at wrist

- 'claw hand' - hyperextension of the metacarpophalangeal joints and flexion at the distal and proximal interphalangeal joints of the 4th and 5th digits
- wasting and paralysis of intrinsic hand muscles (except lateral two lumbricals)
- wasting and paralysis of hypothenar muscles
- sensory loss to the medial 1 1/2 fingers (palmar and dorsal aspects)

### Damage at elbow

- as above (however, ulnar paradox - clawing is more severe in distal lesions)
- radial deviation of wrist

Which one of the following is responsible for the activation of aciclovir?

<input type="radio"/>	A. Guanosine kinase
<input type="radio"/>	B. Protease
<input type="radio"/>	C. Reverse transcriptase
<input type="radio"/>	D. DNA polymerase
<input type="radio"/>	E. Thymidine kinase

Next question

Thymidine kinase phosphorylates aciclovir which then inhibits viral DNA polymerase

### Antiviral agents

#### Aciclovir

- aciclovir is phosphorylated by thymidine kinase which in turn inhibits the viral DNA polymerase

#### Ribavirin

- effective against a range of DNA and RNA viruses
- interferes with the capping of viral mRNA

#### Interferons

- inhibit synthesis of mRNA, translation of viral proteins, viral assembly and release

#### Amantadine

- used to treat influenza
- inhibits uncoating of virus in cell

### Anti-retroviral agent used in HIV

#### Nucleoside analogue reverse transcriptase inhibitors (NRTI)

- examples: zidovudine (AZT), didanosine, lamivudine, stavudine, zalcitabine

#### Protease inhibitors (PI)

- inhibits a protease needed to make the virus able to survive outside the cell
- examples: indinavir, nelfinavir, ritonavir, saquinavir

#### Non-nucleoside reverse transcriptase inhibitors (NNRTI)

- examples: nevirapine, efavirenz

A study looks at adding a new antiplatelet drug in addition to aspirin to patients who've had a stroke. One hundred and seventy patients are enrolled for the study with 120 receiving the new drug in addition to aspirin and the remainder receiving just aspirin. After 5 years 18 people who received the new drug had a further stroke compared to 10 people who just received aspirin. What is the number needed to treat?

- ☐ A. 8
- ☐ B. 15
- ☐ C. 1.8
- ☒ D. 20
- ☐ E. 10

[Next question](#)

$$\text{NNT} = 1 / \text{Absolute Risk Reduction}$$

$$\text{Control event rate} = 10 / 50 = 0.2$$

$$\text{Experimental event rate} = 18 / 120 = 0.15$$

$$\text{Absolute risk reduction} = 0.2 - 0.15 = 0.05$$

$$\text{Number needed to treat} = 1 / 0.05 = 20$$

### Numbers needed to treat and absolute risk reduction

Numbers needed to treat (NNT) is a measure that indicates how many patients would require an intervention to reduce the expected number of outcomes by one

It is calculated by  $1/(\text{Absolute risk reduction})$  and is rounded to the next highest whole number

Experimental event rate (EER) = (Number who had particular outcome with the intervention) / (Total number who had the intervention)

Control event rate (CER) = (Number who had particular outcome with the control/ (Total number who had the control)

### Absolute risk reduction = CER-EER or EER-CER?

The absolute risk reduction (ARR) may be calculated by finding the absolute difference between the control event rate (CER) and the experimental event rate (EER). You will often find both versions of the above listed in different sources. In some ways it doesn't matter which you use as you will end up with the same answer but from a technical point of view:

- if the outcome of the study is undesirable then  $\text{ARR} = \text{CER} - \text{EER}$

- if the outcome of the study is desirable then  $ARR^* = EER - CER$

\*this may be more accurately termed absolute benefit increase, rather than absolute risk reduction

**Question 309 of 402**

Next

A 68-year-old man is admitted with haematemesis. A gastroscopy performed as an inpatient shows a carcinoma which is confirmed on biopsy. Who is the most appropriate person to inform the patient of the diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. The F2 doctor on the ward who has most contact with the patient |
| <input type="radio"/> | B. The doctor who performed the gastroscopy                        |
| <input type="radio"/> | C. His GP following discharge                                      |
| <input type="radio"/> | D. The consultant in-charge of his care                            |
| <input type="radio"/> | E. His next-of-kin after you have told him/her                     |

Next question

One of the key aims of the entrance exam is to assess a doctors ability to act in a compassionate and empathetic way. Many of you may recall incidences of patients being told about a cancer diagnosis in inappropriate circumstances.

The most appropriate person to inform the patient is the consultant in this scenario. He/she is currently in charge of their care and will be best placed to answer questions about management and prognosis. The F2 doctor will be less able to do this but will at least be known to the patient.

The doctor who performed the gastroscopy is unlikely to know the patient apart from their brief meeting prior to the procedure. Asking the GP to tell the patient is a 'cop-out' on a number of levels. Firstly the patient may feel that the hospital team 'could not be bothered' to tell him themselves. Secondly it results in an unnecessary delay and thirdly the GP may not be best placed to give information on management and prognosis.

Telling the next-of-kin is the worst option as it breaks confidentiality.



A 90-year-old man is admitted to hospital. He is taking no regular medication. On admission his blood pressure is 170/68 mmHg. Which one of the following is the main factor which accounts for the large pulse pressure?

<input type="radio"/>	A. Calcified brachial arteries
<input type="radio"/>	B. Autonomic dysfunction
<input type="radio"/>	C. Reduced aortic compliance
<input type="radio"/>	D. Reduced left ventricular ejection fraction
<input type="radio"/>	E. Reduced circulating volume

[Next question](#)

## Cardiovascular physiology

### Left ventricular ejection fraction

Left ventricular ejection fraction = (stroke volume / end diastolic LV volume ) \* 100%

Stroke volume = end diastolic LV volume - end systolic LV volume

### Pulse pressure

Pulse pressure = Systolic Pressure - Diastolic Pressure

Factors which increase pulse pressure

- a less compliant aorta (this tends to occur with advancing age)
- increased stroke volume

What is the typical vital capacity in a male?

- |                       |    |          |
|-----------------------|----|----------|
| <input type="radio"/> | A. | 300 ml   |
| <input type="radio"/> | B. | 500 ml   |
| <input type="radio"/> | C. | 1,500 ml |
| <input type="radio"/> | D. | 2,500 ml |
| <input type="radio"/> | E. | 4,500 ml |

[Next question](#)

### Respiratory physiology: lung volumes

Tidal volume (TV)

- volume inspired or expired with each breath at rest
- 500ml in males, 350ml in females

Inspiratory reserve volume (IRV) = 2-3 L

- maximum volume of air that can be inspired at the end of a normal tidal inspiration
- inspiratory capacity = TV + IRV

Expiratory reserve volume (ERV) = 750ml

- maximum volume of air that can be expired at the end of a normal tidal expiration

Residual volume (RV) = 1.2L

- volume of air remaining after maximal expiration
- increases with age
- $RV = FRC - ERV$

Vital capacity (VC) = 5L

- maximum volume of air that can be expired after a maximal inspiration
- 4,500ml in males, 3,500 mls in females
- decreases with age
- $VC = \text{inspiratory capacity} + ERV$

Total lung capacity (TLC) is the sum of the vital capacity + residual volume

Which one of the following techniques would be most suitable to detect and quantify a viral protein?

- |                       |                              |
|-----------------------|------------------------------|
| <input type="radio"/> | A. Polymerase chain reaction |
| <input type="radio"/> | B. Northern blotting         |
| <input type="radio"/> | C. Western blotting          |
| <input type="radio"/> | D. Southern blotting         |
| <input type="radio"/> | E. Eastern blotting          |

Next question

#### Molecular biology techniques

- SNOW (South - **N**Orth - **W**est)
- DROP (**D**NNA - **R**NA - **P**rotein)

#### Molecular biology techniques

The following table shows a very basic summary of molecular biology techniques

Southern blotting	Detects DNA
Northern blotting	Detects RNA
Western blotting	Detects and quantifies proteins

Which one of the following significance tests is used to analyse data which is measured and follows a normal distribution?

<input type="radio"/>	A. Chi-squared test
<input type="radio"/>	B. Spearman's rank correlation coefficient
<input type="radio"/>	C. Wilcoxon matched-pairs
<input type="radio"/>	D. Mann-Whitney test
<input type="radio"/>	E. Student's t-test

[Next question](#)

Student's t-test is used to analyse parametric data. The other tests are used on non-parametric data

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Which one of the following statements regarding leptin is incorrect?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Is produced mainly by the hypothalamus                   |
| <input type="radio"/> | B. Stimulates the release of melanocyte-stimulating hormone |
| <input type="radio"/> | C. Obese patients have higher leptin levels                 |
| <input type="radio"/> | D. Plays a key role in the regulation of body weight        |
| <input type="radio"/> | E. High levels decrease appetite                            |

Next question

Leptin is secreted by adipose tissue

## Obesity: physiology

### Leptin

Leptin is thought to play a key role in the regulation of body weight. It is produced by adipose tissue and acts on satiety centres in the hypothalamus and decreases appetite. More adipose tissue (e.g. in obesity) results in high leptin levels.

Leptin stimulates the release of melanocyte-stimulating hormone (MSH) and corticotrophin-releasing hormone (CRH). Low levels of leptin stimulates the release of neuropeptide Y (NPY)

### Ghrelin

Where as leptin induces satiety, ghrelin stimulates hunger. It is produced mainly by the fundus of the stomach and the pancreas. Ghrelin levels increase before meals and decrease after meals

A study compares the sensitivity of two tests for colorectal cancer. The first test has a sensitivity of 85% whilst the second test has a sensitivity of 91%. What type of significance test should be used for comparing the two results?

<input type="radio"/>	A. Wilcoxon matched-pairs
<input type="radio"/>	B. Mann-Whitney test
<input type="radio"/>	C. Student's t-test
<input type="radio"/>	D. Chi-squared test
<input type="radio"/>	E. Pearson's test

[Next question](#)

As percentages are being compared the chi-squared test should be used

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
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- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Which one of the following is not a risk factor for the development of pre-eclampsia?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Previous history of pre-eclampsia       |
| <input type="radio"/> | B. Body mass index of 34 kg/m <sup>2</sup> |
| <input type="radio"/> | C. Age of 42 years                         |
| <input type="radio"/> | D. Multiple pregnancy                      |
| <input type="radio"/> | E. Multiparity                             |

Next question

No previous pregnancies is a risk factor for pre-eclampsia. Questions on maternal health during pregnancy are now common in the MRCP

### Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

### Risk factors

- > 40 years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index > 30 kg/m<sup>2</sup>
- diabetes mellitus
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

### Features of severe pre-eclampsia

- hypertension: typically > 170/110 mmHg and proteinuria as above

- proteinuria: dipstick ++/+++
- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count  $< 100 \times 10^6/l$ , abnormal liver enzymes or HELLP syndrome

## Management

- consensus guidelines recommend treating blood pressure  $> 160/110$  mmHg although many clinicians have a lower threshold
- oral labetalol is now first-line following the 2010 NICE guidelines. Nifedipine and hydralazine may also be used
- delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario



Which of the following is true regarding endothelin?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. It is a potent vasodilator  |
| <input type="radio"/> | B. It is produced mainly by pulmonary tissue                           |
| <input type="radio"/> | C. It acts on target cells by stimulating guanylate cyclase            |
| <input type="radio"/> | D. Release is stimulated by nitric oxide                               |
| <input type="radio"/> | E. Endothelin antagonists are useful in primary pulmonary hypertension |

Next question

### Endothelin

Endothelin is a potent, long-acting vasoconstrictor and bronchoconstrictor. It is secreted initially as a prohormone by the vascular endothelium and later converted to ET-1 by the action of endothelin converting enzyme. It acts via interaction with a G-protein linked to phospholipase C leading to calcium release. Endothelin is thought to be important in the pathogenesis of many diseases including primary pulmonary hypertension (endothelin antagonists are now used), cardiac failure, hepatorenal syndrome and Raynaud's

Promotes release

- angiotensin II
- ADH
- hypoxia
- mechanical shearing forces

Inhibits release

- nitric oxide
- prostacyclin

Raised levels in

- MI
- heart failure
- ARF
- asthma
- primary pulmonary hypertension

Which one of the following radiotracers is used during cardiac Positron Emission Tomography (PET) scans?

<input type="radio"/>	A. Gallium
<input type="radio"/>	B. Fluorodeoxyglucose
<input type="radio"/>	C. Technetium (99mTc)
<input type="radio"/>	D. Thallium
<input type="radio"/>	E. Fluorine-18

Next question

### Cardiac imaging: non-invasive techniques excluding echocardiography

The ability to image the heart using non-invasive techniques such as MRI, CT and radionuclides has evolved rapidly over recent years.

#### Nuclear imaging

These techniques use radiotracers which are extracted by normal myocardium. Examples include:

- thallium
- technetium (99mTc) sestamibi: a coordination complex of the radioisotope technetium-99m with the ligand methoxyisobutyl isonitrile (MIBI), used in 'MIBI' or cardiac Single Photon Emission Computed Tomography (SPECT) scans
- fluorodeoxyglucose (FDG): used in Positron Emission Tomography (PET) scans

The primary role of SPECT is to assess myocardial perfusion and myocardial viability. Two sets of images are usually acquired. First the myocardium at rest followed by images of the myocardium during stress (either exercise or following adenosine / dipyridamole). By comparing the rest with stress images any areas of ischaemia can be classified as reversible or fixed (e.g. Following a myocardial infarction). Cardiac PET is predominately a research tool at the current time

#### MUGA

- Multi Gated Acquisition Scan, also known as radionuclide angiography
- radionuclide (technetium-99m) is injected intravenously
- the patient is placed under a gamma camera
- may be performed as a stress test
- can accurately measure left ventricular ejection fraction. Typically used before and after cardiotoxic drugs are used

## **Cardiac Computed Tomography (CT)**

Cardiac CT is useful for assessing suspected ischaemic heart disease, using two main methods:

- calcium score: there is known to be a correlation between the amount of atherosclerotic plaque calcium and the risk of future ischaemic events. Cardiac CT can quantify the amount of calcium producing a 'calcium score'
- contrast enhanced CT: allows visualisation of the coronary artery lumen

If these two techniques are combined cardiac CT has a very high negative predictive value for ischaemic heart disease.

## **Cardiac MRI**

Cardiac MRI (commonly termed CMR) has become the gold standard for providing structural images of the heart. It is particularly useful when assessing congenital heart disease, determining right and left ventricular mass and differentiating forms of cardiomyopathy. Myocardial perfusion can also be assessed following the administration of gadolinium. Currently CMR provides limited data on the extent of coronary artery disease.

Please also see the British Heart Foundation link for an excellent summary.

Which of the following conditions is NOT inherited in a X-linked recessive fashion:

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Myotonic dystrophy |
| <input type="radio"/> | B. G6PD deficiency    |
| <input type="radio"/> | C. Haemophilia B      |
| <input type="radio"/> | D. Colour blindness   |
| <input type="radio"/> | E. Fabry's disease    |

Next question

X-linked conditions: Duchenne/Becker, haemophilia, G6PD

### X-linked recessive conditions

The following conditions are inherited in a X-linked recessive fashion:

Androgen insensitivity syndrome  
Becker muscular dystrophy  
Colour blindness  
Duchenne muscular dystrophy  
Fabry's disease  
G6PD deficiency  
Haemophilia A,B  
Hunter's disease  
Lesch-Nyhan syndrome  
Nephrogenic diabetes insipidus  
Ocular albinism  
Retinitis pigmentosa  
Wiskott-Aldrich syndrome

The following diseases have varying patterns of inheritance, with the majority being in an X-linked recessive fashion:

Chronic granulomatous disease (in > 70%)

Which one of the following conditions is NOT an autosomal recessive condition?

<input type="radio"/>	A. Haemochromatosis
<input type="radio"/>	B. PKU
<input type="radio"/>	C. Hereditary spherocytosis
<input type="radio"/>	D. Tay-Sach's
<input type="radio"/>	E. Friedreich's ataxia

Next question

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

Hereditary spherocytosis is inherited in an autosomal dominant fashion.

### Autosomal recessive conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal recessive:

- Albinism
- Ataxia telangiectasia
- Congenital adrenal hyperplasia
- Cystic fibrosis
- Cystinuria
- Familial Mediterranean Fever
- Fanconi anaemia
- Friedreich's ataxia
- Gilbert's syndrome\*
- Glycogen storage disease
- Haemochromatosis
- Homocystinuria
- Lipid storage disease: Tay-Sach's, Gaucher, Niemann-Pick
- Mucopolysaccharidoses: Hurler's

- PKU
- Sickle cell anaemia
- Thalassaemias
- Wilson's disease

\*this is still a matter of debate and many textbooks will list Gilbert's as autosomal dominant

Which one of the following is least associated with homocystinuria?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Recurrent renal stones     |
| <input type="radio"/> | B. Downwards lens dislocation |
| <input type="radio"/> | C. Deep vein thrombosis       |
| <input type="radio"/> | D. Arachnodactyly             |
| <input type="radio"/> | E. Learning difficulties      |

Next question

Cystinuria not homocystinuria is associated with recurrent renal stones

### Homocystinuria

Homocystinuria is a rare autosomal recessive disease caused by deficiency of cystathionine beta synthase. This results in an accumulation of homocysteine which is then oxidized to homocystine.

#### Features

- often patients have fine, fair hair
- musculoskeletal: may be similar to Marfan's - arachnodactyly etc
- neurological patients may have learning difficulties, seizures
- ocular: downwards (inferonasal) dislocation of lens
- increased risk of arterial and venous thromboembolism
- also malar flush, livedo reticularis

Diagnosis is made by the cyanide-nitroprusside test, which is also positive in cystinuria

Treatment is vitamin B6 (pyridoxine) supplements

Which one of the following foodstuff contains the most energy per unit weight?

- |                       |               |
|-----------------------|---------------|
| <input type="radio"/> | A. Pasta      |
| <input type="radio"/> | B. Cheese     |
| <input type="radio"/> | C. Butter     |
| <input type="radio"/> | D. Peanuts    |
| <input type="radio"/> | E. White rice |

Next question

Butter is a type of fat and therefore contains the most energy.

### Food energy

The amount of energy a food product contains is expressed in calories (kcal).

In simple terms, per unit weight, fats contain twice as many calories as protein or carbohydrates.



**Question 323 of 402**

Next

You are a ST1 doctor on a medical ward. It is 5:15pm and you were scheduled to finish your day 15 minutes ago. Today you're particularly keen to leave as it is your wife's birthday and you've arranged a night out. One of the staff nurses bleeps you as Mr Jones, one of your patients, has become drowsy. He was admitted two days ago to your ward with an exacerbation of COPD. What is the most appropriate course of action?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Bleep the on-call doctor yourself and ask him to review  |
| <input type="radio"/> | B. Tell her to try decreasing his oxygen to 24% and see how he is in 30 minutes                             |
| <input type="radio"/> | C. Tell the nurse to bleep the on-call doctor   |
| <input type="radio"/> | D. Tell the nurse to bleep the on-call doctor + fill in a clinical incident form as you bleeped after hours |
| <input type="radio"/> | E. Go and assess the patient yourself   |

Next question

This question is mainly about professionalism and 'putting the patient first'.

The most appropriate response is to go and assess the patient yourself. You are most likely to know their history and it is possible that the on-call doctor will be delayed in reaching the ward due to other patients. The next best option is to bleep the on-call doctor yourself. This allows for a proper hand-over, which would not happen if you asked the nurse to bleep the on-call doctor.

Filling in a clinical incident form as you were bleeped after hours is not appropriate.

The worst response would be to ask the nurse to instigate medical treatment without first assessing the patient. This is clearly dangerous.

Which one of the following statements regarding the use of the p-value in statistical hypothesis testing is correct?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. The p-value is the probability that the null hypothesis is true                                   |
| <input type="radio"/> | B. $1 - (\text{p-value})$ is the probability of the alternative hypothesis being true                |
| <input type="radio"/> | C. The null hypothesis is rejected if the p-value is smaller than or equal to the significance level |
| <input type="radio"/> | D. The p-value is the probability that a replicating experiment would not yield the same conclusion  |
| <input type="radio"/> | E. The p-value is equal to the probability of making a type II error                                 |

Next question

### Significance tests

A null hypothesis ( $H_0$ ) states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct.

For example:

- 'there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not'

The alternative hypothesis ( $H_1$ ) is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

The **p value** is the probability of obtaining a result by chance at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. It is therefore equal to the chance of making a type I error (see below).

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist, a false positive. This is determined against a preset significance level (termed alpha). As the significance level is determined in advance the chance of making a type I error is not affected by sample size. It is however increased if the number of end-points are increased. For example if a study has 20 end-points it is likely one of these will be reached, just by chance.
- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists, a false negative. The probability of making a type II error is termed beta. It is determined by both sample size and alpha

	Study accepts $H_0$	Study rejects $H_0$
Reality $H_0$		Type 1 error (alpha)
Reality $H_1$	Type 2 error (beta)	Power (1 - beta)

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false, i.e. the probability of detecting a statistically significant difference

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

A 54-year-old woman is admitted to the Medical Admissions Unit following a collapse. Bloods taken on admission show the following:

Magnesium	0.40 mmol/l
-----------	-------------

Which one of the following factors is most likely to be responsible for this result?

<input type="radio"/>	A. Excessive resuscitation with intravenous saline
<input type="radio"/>	B. Frusemide therapy
<input type="radio"/>	C. Digoxin therapy
<input type="radio"/>	D. Rhabdomyolysis
<input type="radio"/>	E. Hypothermia

Next question

## Hypomagnesaemia

Cause of low magnesium

- diuretics
- total parenteral nutrition
- diarrhoea
- alcohol
- hypokalaemia, hypocalcaemia

Features

- paraesthesia
- tetany
- seizures
- arrhythmias
- decreased PTH secretion --> hypocalcaemia
- ECG features similar to those of hypokalaemia
- exacerbates digoxin toxicity

Each one of the following is seen in Wiskott-Aldrich syndrome, except:

<input type="radio"/>	A. Thrombocytopenia
<input type="radio"/>	B. Recurrent chest infections
<input type="radio"/>	C. X-linked recessive inheritance
<input type="radio"/>	D. Mutation in the WASP gene
<input type="radio"/>	E. Psoriasis

Next question

### Wiskott-Aldrich syndrome

Wiskott-Aldrich syndrome causes primary immunodeficiency due to a combined B- and T-cell dysfunction. It is inherited in a X-linked recessive fashion and is thought to be caused by mutation in the WASP gene.

#### Features

- recurrent bacterial infections (e.g. Chest)
- eczema
- thrombocytopaenia
- low IgM levels

Why do patients with chronic kidney disease have a raised phosphate level?

<input type="radio"/>	A. Decreased renal excretion
<input type="radio"/>	B. Increased gut absorption
<input type="radio"/>	C. Hypervitaminosis D
<input type="radio"/>	D. Primary hyperparathyroidism
<input type="radio"/>	E. Decreased 25-alpha hydroxylation of vitamin D

Next question

### Chronic kidney disease: bone disease

Basic problems in chronic kidney disease

- low vitamin D (1-alpha hydroxylation normally occurs in the kidneys)
- high phosphate
- low calcium: due to lack of vitamin D, high phosphate
- secondary hyperparathyroidism: due to low calcium, high phosphate and low vitamin D

Several clinical manifestations may result:

Osteitis fibrosa cystica

- aka hyperparathyroid bone disease

Adynamic

- reduction in cellular activity (both osteoblasts and osteoclasts) in bone
- may be due to over treatment with vitamin D

Osteomalacia

- due to low vitamin D

Osteosclerosis

Osteoporosis

Which of the following statements is true regarding the standard polymerase chain reaction (PCR)?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Restriction endonuclease enzymes are applied to DNA fragments prior to electrophoresis |
| <input type="radio"/> | B. PCR use is limited by its relatively low sensitivity                                   |
| <input type="radio"/> | C. A thermostable DNA polymerase is required  |
| <input type="radio"/> | D. PCR is currently limited to prenatal diagnosis and forensics                           |
| <input type="radio"/> | E. A single DNA oligonucleotide primer is necessary                                       |

Next question

## PCR

Polymerase chain reaction (PCR) is a molecular genetic investigation technique. The main advantage of PCR is its sensitivity: only one strand of sample DNA is needed to detect a particular DNA sequence. It now has many uses including prenatal diagnosis, detection of mutated oncogenes and diagnosis of infections. PCR is also extensively used in forensics. Prior to the procedure it is necessary to have two DNA oligonucleotide primers. These are complimentary to specific DNA sequences at either end of the target DNA

Initial prep

- sample of DNA is added to test tube along with two DNA primers
- a thermostable DNA polymerase (Taq) is added

The following cycle then takes place

- mixture is heated to almost boiling point causing denaturing (uncoiling) of DNA
- mixture is then allowed to cool: complimentary strands of DNA pair up, as there is an excess of the primer sequences they pair with DNA preferentially

The above cycle is then repeated, with the amount of DNA doubling each time

Reverse transcriptase PCR

- used to amplify RNA
- RNA is converted to DNA by reverse transcriptase
- gene expression in the form of mRNA (rather than the actual DNA sequence) can therefore be analyzed

Which one of the following statements regarding galactosaemia is incorrect?

<input type="radio"/>	A. Autosomal recessive inheritance
<input type="radio"/>	B. May cause cataracts
<input type="radio"/>	C. Caused by the absence of galactose-1-phosphate uridyl transferase
<input type="radio"/>	D. May cause jaundice
<input type="radio"/>	E. May cause peripheral neuropathy

Next question

### Galactosaemia

Galactosaemia is a rare autosomal recessive condition caused by the absence of galactose-1-phosphate uridyl transferase. This results in intracellular accumulation of galactose-1-phosphate

#### Features

- jaundice
- failure to thrive
- hepatomegaly
- cataracts
- hypoglycaemia after exposure to galactose
- Fanconi syndrome

#### Diagnosis

- urine reducing substances

Management is with a galactose free diet



Looser's zones x-ray are most characteristically associated with which one of the following conditions?

<input type="radio"/>	A. Primary hyperparathyroidism
<input type="radio"/>	B. Hypoparathyroidism
<input type="radio"/>	C. Osteomalacia
<input type="radio"/>	D. Paget's disease
<input type="radio"/>	E. Osteoporosis

[Next question](#)

## Osteomalacia

### Basics

- normal bony tissue but decreased mineral content
- rickets if when growing
- osteomalacia if after epiphysis fusion

### Types

- vitamin D deficiency e.g. malabsorption, lack of sunlight, diet
- renal failure
- drug induced e.g. anticonvulsants
- vitamin D resistant; inherited
- liver disease, e.g. cirrhosis

### Features

- rickets: knock-knee, bow leg, features of hypocalcaemia
- osteomalacia: bone pain, fractures, muscle tenderness, proximal myopathy

### Investigation

- low calcium, phosphate, 25(OH) vitamin D
- raised alkaline phosphatase
- x-ray: children - cupped, ragged metaphyseal surfaces; adults - translucent bands (Looser's zones or pseudofractures)

### Treatment

- calcium with vitamin D tablets

Which of the following statements is true regarding X-linked recessive inheritance?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. A female child of a heterozygous female carrier has a 50% chance of being a carrier |
| <input type="radio"/> | B. An example is Friedreich's ataxia   |
| <input type="radio"/> | C. 50% of the male offspring of affected males will manifest the disease               |
| <input type="radio"/> | D. An affected child's uncle on the paternal side will also manifest the disease       |
| <input type="radio"/> | E. 50% of the female offspring of affected males will be carriers                      |

Next question

### X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters.

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier.

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen.

**Question 332 of 402**

Next

A 61-year-old female who has recently emigrated from the Indian subcontinent presents with muscle weakness. Bloods reveal a low serum calcium. A diagnosis of osteomalacia is suspected. Which one of the following, per average serving, provides the best source of vitamin D?

<input type="radio"/>	A. Lentils
<input type="radio"/>	B. Sunflower seeds
<input type="radio"/>	C. Salmon
<input checked="" type="radio"/>	D. Cod liver oil
<input type="radio"/>	E. Milk

Cod liver oil provides around 1,300 IU per 15 ml serving

**Vitamin deficiency**

The table below summarises vitamin deficiency states

Vitamin	Chemical name	Deficiency state
A	Retinoids	Night-blindness (nyctalopia)
B1	Thiamine	Beriberi <ul style="list-style-type: none"><li>• polyneuropathy, Wernicke-Korsakoff syndrome</li><li>• heart failure</li></ul>
B3	Niacin	Pellagra <ul style="list-style-type: none"><li>• dermatitis</li><li>• diarrhoea</li><li>• dementia</li></ul>
B6	Pyridoxine	Anaemia, irritability, seizures
B7	Biotin	Dermatitis, seborrhoea
B9	Folic acid	Megaloblastic anaemia, deficiency during pregnancy - neural tube defects
B12	Cyanocobalamin	Megaloblastic anaemia, peripheral neuropathy
C	Ascorbic acid	Scurvy <ul style="list-style-type: none"><li>• gingivitis</li><li>• bleeding</li></ul>
D	Ergocalciferol, cholecalciferol	Rickets, osteomalacia
E	Tocopherol, tocotrienol	Mild haemolytic anaemia in newborn infants, ataxia, peripheral neuropathy
K	Naphthoquinone	Haemorrhagic disease of the newborn, bleeding diathesis

**Question 333 of 402**

Next

You are asked for advice from a local GP. He has received the following blood results for one of his patients, a 50-year-old non-smoker.

Na <sup>+</sup>	130 mmol/l
K <sup>+</sup>	4.2 mmol/l
Bicarbonate	23 mmol/l
Urea	4.8 mmol/l
Creatinine	71 µmol/l

Which one of his medications is most likely to explain this result?

- ☐ A. Fluoxetine
- ☐ B. Pioglitazone
- ☐ C. Methotrexate
- ☐ D. Losartan
- ☐ E. Nicorandil

Next question

SIADH - drug causes: carbamazepine, sulfonylureas, SSRIs, tricyclics

**SIADH: causes****Malignancy**

- especially small cell lung cancer
- also: pancreas, prostate

**Neurological**

- stroke
- subarachnoid haemorrhage
- subdural haemorrhage
- meningitis/encephalitis/abscess

**Infections**

- tuberculosis
- pneumonia

## Drugs

- sulfonylureas
- SSRIs, tricyclics
- carbamazepine
- vincristine
- cyclophosphamide

## Other causes

- positive end-expiratory pressure (PEEP)
- porphyrias

Which one of the following cell types secretes the majority of pulmonary surfactant?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Type II pneumocytes |
| <input type="radio"/> | B. Kupffer cells       |
| <input type="radio"/> | C. Type I pneumocytes  |
| <input type="radio"/> | D. Macrophages         |
| <input type="radio"/> | E. Elastocytes         |

Next question

### Pulmonary surfactant

Surfactant is a mixture of phospholipids, carbohydrates and proteins released by type 2 pneumocytes. The main functioning component is dipalmitoyl phosphatidylcholine (DPPC) which reduces alveolar surface tension.

#### Basics

- first detectable around 28 weeks
- as alveoli decrease in size, surfactant concentration is increased, helping prevent the alveoli from collapsing
- reduces the muscular force needed to expand the lungs (i.e. decreases the work of breathing)
- lowers the elastic recoil at low lung volumes and thus helps to prevent the alveoli from collapsing at the end of each expiration

Which one of the following statements concerning altitude related disorders is true?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Symptoms typically start to develop above 1,500m                               |
| <input type="radio"/> | B. Physical fitness protects against altitude related disorders                   |
| <input type="radio"/> | C. High altitude pulmonary oedema should be treated with frusemide first-line     |
| <input type="radio"/> | D. Acute mountain sickness is generally a self-limiting condition                 |
| <input type="radio"/> | E. Symptoms of acute mountain sickness develop within 4 hours of gaining altitude |

Next question

### Altitude related disorders

There are three main types of altitude related disorders: acute mountain sickness (AMS), which may progress to high altitude pulmonary edema (HAPE) or high altitude cerebral edema (HACE). All three conditions are due to the chronic hypobaric hypoxia which develops at high altitudes

Acute mountain sickness is generally a self-limiting condition. Features of AMS start to occur above 2,500 - 3,000m, developing gradually over 6-12 hours and potentially last a number of days:

- headache
- nausea
- fatigue

#### Prevention and treatment of AMS

- the risk of AMS may actually be positively correlated to physical fitness
- gain altitude at no more than 500 m per day
- acetazolamide (a carbonic anhydrase inhibitor) is widely used to prevent AMS and has a supporting evidence base
- treatment: descent

A minority of people above 4,000m go onto develop high altitude pulmonary oedema (HAPE) or high altitude cerebral oedema (HACE), potentially fatal conditions

- HAPE presents with classical pulmonary oedema features
- HACE presents with headache, ataxia, papilloedema

#### Management of HACE

- descent
- dexamethasone

#### Management of HAPE

- descent
- nifedipine, dexamethasone, acetazolamide, phosphodiesterase type V inhibitors\*
- oxygen if available

\*the relative merits of these different treatments has only been studied in small trials. All seem to work by reducing systolic pulmonary artery pressure



Which one of the following features is not associated with Turner's syndrome?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Short stature            |
| <input type="radio"/> | B. High-arched palate       |
| <input type="radio"/> | C. Coarctation of the aorta |
| <input type="radio"/> | D. Webbed neck              |
| <input type="radio"/> | E. Secondary amenorrhoea    |

Next question

Primary, not secondary, amenorrhoea is seen in Turner's syndrome

### Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

#### Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

A 68-year-old woman presents with lethargy and generalised aches. As part of a blood screen the following results are obtained:

Calcium	2.83 mmol/l
Albumin	42 g/l
ESR	26 mm/hr

What is the most likely cause of these blood results?

- ☐ A. Multiple myeloma
- ☐ B. Sarcoidosis
- ☐ C. Normal
- ☐ D. Breast cancer metastases
- ☐ E. Primary hyperparathyroidism

Next question

This question tests whether you have an understanding of the incidence of common disorders. All of the above may cause hypercalcaemia but cancer and primary hyperparathyroidism are the most common causes in this age group. A normal ESR (given her age) points towards a diagnosis of primary hyperparathyroidism.

### Hypercalcaemia: causes

The most common causes of hypercalcaemia are malignancy (bone metastases, myeloma, PTHrP from squamous cell lung cancer) and primary hyperparathyroidism

Other causes include

- sarcoidosis\*
- vitamin D intoxication
- acromegaly
- thyrotoxicosis
- Milk-alkali syndrome
- drugs: thiazides, calcium containing antacids
- dehydration
- Addison's disease
- Paget's disease of the bone\*\*

\*other causes of granulomas may lead to hypercalcaemia e.g. Tuberculosis and histoplasmosis

\*\*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

A study looks at whether a new oral treatment for patients with heart failure can prevent hospital admissions. When reviewing the data how should it be decided if the test was statistically significant?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. $p\text{-value} < 2 \text{ standard deviates from mean}$ |
| <input type="radio"/> | B. $p\text{-value} < (1 - \text{type II error})$            |
| <input type="radio"/> | C. $p\text{-value} < \text{significance level}$             |
| <input type="radio"/> | D. $p\text{-value} < \text{power}$                          |
| <input type="radio"/> | E. $p\text{-value} < 0.01$                                  |

[Next question](#)

The significance level of a test is defined as the probability of rejecting the null hypothesis when the null hypothesis is actually true (a Type I error). It is often represented by the Greek symbol alpha.

A study is only statistically significant if the p-value reaches the significance level set before the study is started. Popular levels of significance are 5% (0.05), 1% (0.01) and 0.1% (0.001).

### Significance tests

A null hypothesis ( $H_0$ ) states that two treatments are equally effective (and is hence negatively phrased). A significance test uses the sample data to assess how likely the null hypothesis is to be correct.

For example:

- 'there is no difference in the prevalence of colorectal cancer in patients taking low-dose aspirin compared to those who are not'

The alternative hypothesis ( $H_1$ ) is the opposite of the null hypothesis, i.e. There is a difference between the two treatments

The **p value** is the probability of obtaining a result by chance at least as extreme as the one that was actually observed, assuming that the null hypothesis is true. It is therefore equal to the chance of making a type I error (see below).

Two types of errors may occur when testing the null hypothesis

- type I: the null hypothesis is rejected when it is true - i.e. Showing a difference between two groups when it doesn't exist, a false positive. This is determined against a preset significance level (termed alpha). As the significance level is determined in advance the chance of making a type I error is not affected by sample size. It is however increased if the number of end-points are increased. For example if a study has 20 end-points it is likely one of these will be reached, just by chance.

- type II: the null hypothesis is accepted when it is false - i.e. Failing to spot a difference when one really exists, a false negative. The probability of making a type II error is termed beta. It is determined by both sample size and alpha

	Study accepts $H_0$	Study rejects $H_0$
Reality $H_0$		Type 1 error (alpha)
Reality $H_1$	Type 2 error (beta)	Power (1 - beta)

The power of a study is the probability of (correctly) rejecting the null hypothesis when it is false, i.e. the probability of detecting a statistically significant difference

- power = 1 - the probability of a type II error
- power can be increased by increasing the sample size

Which of the following statements is true regarding autosomal dominant inheritance?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Individuals who are symptomatic of the disease always have parents who are symptomatic of the disease |
| <input type="radio"/> | B. Only heterozygotes manifest disease   |
| <input type="radio"/> | C. 50% of children will be carriers  |
| <input type="radio"/> | D. Responsible for the majority of enzyme deficiency disorders   |
| <input type="radio"/> | E. The risk remains the same for each successive pregnancy   |

Next question

Due to non-penetrance affected individuals do not always have affected parents

### Autosomal dominant

In autosomal dominant diseases:

- both homozygotes and heterozygotes manifest disease (there is no carrier state)
- both males and females affected
- only affected individuals can pass on disease
- disease is passed on to 50% of children
- normally appears in every generation (although see below)
- risk remains same for each successive pregnancy

Complicating factors:

- non-penetrance: lack of clinical signs and symptoms (normal phenotype) despite abnormal gene. E.g. 40% otosclerosis
- spontaneous mutation: new mutation in one of gametes e.g. 80% of individuals with achondroplasia have unaffected parents

Which one of the following statements regarding hypocalcaemia is incorrect?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Most features are a result of neuromuscular excitability             |
| <input type="radio"/> | B. Chronic hypocalcaemia may cause cataracts                            |
| <input type="radio"/> | C. Perioral paraesthesia is seen  |
| <input type="radio"/> | D. Chvostek's sign is more sensitive and specific than Trousseau's sign |
| <input type="radio"/> | E. Prolonged QT interval is seen  |

Next question

Hypocalcaemia: Trousseau's sign is more sensitive and specific than Chvostek's sign

### Hypocalcaemia: features

As extracellular calcium concentrations are important for muscle and nerve function many of the features seen in hypocalcaemia seen a result of neuromuscular excitability

#### Features

- tetany: muscle twitching, cramping and spasm
- perioral paraesthesia
- if chronic: depression, cataracts
- ECG: prolonged QT interval

#### Trousseau's sign

- carpal spasm if the brachial artery occluded by inflating the blood pressure cuff and maintaining pressure above systolic
- wrist flexion and fingers drawn together
- seen in around 95% of patients with hypocalcaemia and around 1% of normocalcaemic people

#### Chvostek's sign

- tapping over parotid causes facial muscles to twitch
- seen in around 70% of patients with hypocalcaemia and around 10% of normocalcaemic people

Each one of the following features is seen in phenylketonuria, except:

<input type="radio"/>	A. Learning difficulties
<input type="radio"/>	B. Seizures
<input type="radio"/>	C. Eczema
<input type="radio"/>	D. Recurrent infections
<input type="radio"/>	E. 'Musty' urine

[Next question](#)

## Phenylketonuria

Phenylketonuria (PKU) is an autosomal recessive condition caused by a disorder of phenylalanine metabolism. This is due to defect in phenylalanine hydroxylase, an enzyme which converts phenylalanine to tyrosine. High levels of phenylalanine lead to problems such as learning difficulties and seizures. The gene for phenylalanine hydroxylase is located on chromosome 12.

The incidence of PKU is c. 1 in 10,000 live births

### Features

- usually presents by 6 months e.g. with developmental delay
- child classically has fair hair and blue eyes
- learning difficulties
- seizures, typically infantile spasms
- eczema
- 'musty' odour to urine and sweat\*

### Diagnosis

- Guthrie test: the 'heel-prick' test done at 5-9 days of life - also looks for other biochemical disorders such as hypothyroidism
- hyperphenylalaninaemia
- phenylpyruvic acid in urine

### Management

- poor evidence base to suggest strict diet prevents learning disabilities
- dietary restrictions are however important during pregnancy as genetically normal fetuses may be affected by high maternal phenylalanine levels

\*secondary to phenylacetate, a phenylketone

Which one of the following statements is true regarding monoclonal antibodies?

<input type="radio"/>	A. They are produced by the polymerase chain reaction
<input type="radio"/>	B. Infliximab is useful in chronic lymphocytic leukaemia
<input type="radio"/>	C. A hybridoma is a combination of human spleen cells and mouse B-cells
<input type="radio"/>	D. The constant region of the antibody is human in origin
<input type="radio"/>	E. Alemtuzumab is used in the prevention of ischaemic events in patients undergoing percutaneous coronary interventions

Next question

### Monoclonal antibodies

Monoclonal antibodies have an increasing role in medicine. They are manufactured by a technique called somatic cell hybridization. This involves the fusion of myeloma cells with spleen cells from a mouse that has been immunized with the desired antigen. The resulting fused cells are termed a hybridoma and act as a 'factory' for producing monoclonal antibodies. The main limitation to this is that mouse antibodies are immunogenic leading to the formation of human anti-mouse antibodies (HAMAs). This problem is overcome by combining the variable region from the mouse body with the constant region from a human antibody.

Clinical examples of monoclonal antibodies:

- infliximab (anti-TNF): used in rheumatoid arthritis and Crohn's
- rituximab (anti-CD20): used in non-Hodgkin's lymphoma and rheumatoid arthritis
- cetuximab (anti epidermal growth factor receptor): used in metastatic colorectal cancer and head and neck cancer
- trastuzumab (anti-HER2, an EGF receptor): used in metastatic breast cancer
- alemtuzumab (anti-CD52): used in chronic lymphocytic leukaemia
- abciximab (anti-glycoprotein IIb/IIIa receptor): prevention of ischaemic events in patients undergoing percutaneous coronary interventions
- OKT3 (anti-CD3): used to prevent organ rejection

Monoclonal antibodies are also used for:

- medical imaging when combined with a radioisotope
- identification of cell surface markers in biopsied tissue
- diagnosis of viral infections



A study is designed to look at the efficacy of a mandible advancement device in reducing snoring. The severity of snoring was assessed by the partner using a 10 point scale before and after using the device. Fifty people were involved in the study. What is the most appropriate statistical test to apply to this data?

<input type="radio"/>	A. Unpaired Student's t-test
<input type="radio"/>	B. Pearson's product-moment coefficient
<input type="radio"/>	C. Wilcoxon signed-rank test
<input type="radio"/>	D. Chi-squared test
<input type="radio"/>	E. Mann-Whitney test

[Next question](#)

The data in this study is non-parametric, paired and comes from the same population. These factors make the Wilcoxon signed-rank test the most appropriate statistical hypothesis test to use.

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

**Question 344 of 402**

Next

A 33-year-old pregnant woman presents for advice. She is known to have polycystic kidney disease but is currently well. Her father also has polycystic kidneys and is on dialysis . What is the chance her child will also have the disease?

<input type="radio"/>	A. 50% if male
<input type="radio"/>	B. 50%
<input type="radio"/>	C. 25%
<input type="radio"/>	D. 0%
<input type="radio"/>	E. 100%

Next question

Polycystic kidney disease is usually inherited in an autosomal dominant fashion and hence 50% of her children will be affected, regardless of gender. The autosomal recessive form is rare and usually causes death in childhood.

**ADPKD**

Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited cause of kidney disease, affecting 1 in 1,000 Caucasians. Two disease loci have been identified, PKD1 and PKD2, which code for polycystin-1 and polycystin-2 respectively

ADPKD type 1	ADPKD type 2
85% of cases	15% of cases
Chromosome 16	Chromosome 4
Presents with renal failure earlier	

The screening investigation for relatives is abdominal ultrasound:

Ultrasound diagnostic criteria (in patients with positive family history)

- two cysts, unilateral or bilateral, if aged < 30 years
- two cysts in both kidneys if aged 30-59 years
- four cysts in both kidneys if aged > 60 years

Which one of the following statements is true regarding interferon?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Interferon-beta is produced by leucocytes  |
| <input type="radio"/> | B. Interferon-alpha and interferon-beta bind to the same type of receptor   |
| <input type="radio"/> | C. Interferon-gamma has stronger antiviral action than interferon-alpha   |
| <input type="radio"/> | D. Interferon-alpha has been shown to reduce the frequency of exacerbations in patients with relapsing-remitting multiple sclerosis |
| <input type="radio"/> | E. Interferon-gamma has a role in chronic hepatitis C   |

Next question

## Interferon

Interferons (IFN) are cytokines released by the body in response to viral infections and neoplasia. They are classified according to cellular origin and the type of receptor they bind to. IFN-alpha and IFN-beta bind to type 1 receptors whilst IFN-gamma binds only to type 2 receptors.

### IFN-alpha

- produced by leucocytes
- antiviral action
- useful in hepatitis B & C, Kaposi's sarcoma, metastatic renal cell cancer, hairy cell leukaemia
- adverse effects include flu-like symptoms and depression

### IFN-beta

- produced by fibroblasts
- antiviral action
- reduces the frequency of exacerbations in patients with relapsing-remitting MS

### IFN-gamma

- produced by T lymphocytes & NK cells
- weaker antiviral action, more of a role in immunomodulation particularly macrophage activation
- may be useful in chronic granulomatous disease and osteopetrosis

A nurse who is known to have an allergy to latex develops a widespread urticarial rash and facial oedema shortly after eating lunch. Which food is she most likely to have consumed?

<input type="radio"/>	A. Orange
<input type="radio"/>	B. Apple
<input type="radio"/>	C. Grapes
<input type="radio"/>	D. Pear
<input type="radio"/>	E. Banana

[Next question](#)

The nurse is likely to suffer from latex-fruit syndrome.

### Latex allergy

Sensitivity to latex may cause a number of problems:

- type I hypersensitivity (anaphylaxis)
- type IV hypersensitivity (allergic contact dermatitis)
- irritant contact dermatitis

Latex allergy is more common in children with myelomeningocele spina bifida.

### Latex-fruit syndrome

It is recognised that many people who are allergic to latex are also allergic to fruits, particularly banana, pineapple, avocado, chestnut, kiwi fruit, mango, passion fruit and strawberry.

A study is performed to find the normal reference range for IgE levels in adults. Assuming IgE levels follow a normal distribution, what percentage of adults will have an IgE level higher than 2 standard deviations from the mean?

<input type="radio"/>	A. 1.25%
<input type="radio"/>	B. 2.3%
<input type="radio"/>	C. 1.96%
<input type="radio"/>	D. 5%
<input type="radio"/>	E. 0.5%

[Next question](#)

For normally distributed data 95.4% of values lie within 2 standard deviations of the mean, leaving 4.6% outside this range. Therefore 2.3% of values will be higher and 2.3% will be lower than 2 standard deviations from the mean. This figure is sometimes approximated to 2.5%

### Normal distribution

The normal distribution is also known as the Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

#### Properties of the Normal distribution

- symmetrical i.e. Mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 \* SD) to the mean + (1.96 \* SD) is called the 95% confidence interval, i.e. If a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

#### Standard deviation

- the standard deviation (SD) is a measure of how much dispersion exists from the mean
- SD = square root (variance)

An elderly patient with a history of atrial fibrillation develops torsades de pointes shortly after being started on sotalol. What effect does sotalol have on the cardiac cell membrane to make this more likely?

- ☐ A. Blockage of sodium channels
- ☐ B. Opening of potassium channels
- ☐ C. Blockage of potassium channels
- ☐ D. Opening of calcium channels
- ☐ E. Opening of sodium channels

[Next question](#)

Long QT syndrome - usually due to loss-of-function/blockage of K<sup>+</sup> channels

This patient is likely to have developed torsades de pointes secondary to a prolonged QT interval.

### Long QT syndrome

Long QT syndrome (LQTS) is an inherited condition associated with delayed repolarization of the ventricles. It is important to recognise as it may lead to ventricular tachycardia and can therefore cause collapse/sudden death. The most common variants of LQTS (LQT1 & LQT2) are caused by defects in the alpha subunit of the slow delayed rectifier potassium channel. A normal corrected QT interval is less than 430 ms in males and 450 ms in females.

Causes of a prolonged QT interval:

Congenital	Drugs*	Other
<ul style="list-style-type: none"> <li>Jervell-Lange-Nielsen syndrome (includes deafness and is due to an abnormal potassium channel)</li> <li>Romano-Ward syndrome (no deafness)</li> </ul>	<ul style="list-style-type: none"> <li>amiodarone, sotalol, class 1a antiarrhythmic drugs</li> <li>tricyclic antidepressants, selective serotonin reuptake inhibitors (especially citalopram)</li> <li>methadone</li> <li>chloroquine</li> <li>terfenadine**</li> <li>erythromycin</li> </ul>	<ul style="list-style-type: none"> <li>electrolyte: hypocalcaemia, hypokalaemia, hypomagnesaemia</li> <li>acute myocardial infarction</li> <li>myocarditis</li> <li>hypothermia</li> <li>subarachnoid haemorrhage</li> </ul>

### Features

- may be picked up on routine ECG or following family screening
- Long QT1 - usually associated with exertional syncope, often swimming
- Long QT2 - often associated with syncope occurring following emotional stress, exercise or auditory stimuli

- Long QT3 - events often occur at night or at rest
- sudden cardiac death

## Management

- avoid drugs which prolong the QT interval and other precipitants if appropriate (e.g. Strenuous exercise)
- beta-blockers\*\*\*
- implantable cardioverter defibrillators in high risk cases

\*the usual mechanism by which drugs prolong the QT interval is blockage of potassium channels. See the link for more details

\*\*a non-sedating antihistamine and classic cause of prolonged QT in a patient, especially if also taking P450 enzyme inhibitor, e.g. Patient with a cold takes terfenadine and erythromycin at the same time

\*\*\*note sotalol may exacerbate long QT syndrome

Which one of the following diseases is most strongly associated with HLA antigen DR2?

<input type="radio"/>	A. Haemochromatosis
<input type="radio"/>	B. Type 1 diabetes mellitus
<input type="radio"/>	C. Goodpasture's syndrome
<input type="radio"/>	D. Behcet's disease
<input type="radio"/>	E. Coeliac disease

Next question

### HLA associations

HLA antigens are encoded for by genes on chromosome 6. HLA A, B and C are class I antigens whilst DP, DQ, DR are class II antigens. Questions are often based around which diseases have strong HLA associations. The most important associations are listed below:

#### HLA-A3

- haemochromatosis

#### HLA-B5

- Behcet's disease

#### HLA-B27

- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

#### HLA-DQ2/DQ8

- coeliac disease

#### HLA-DR2

- narcolepsy
- Goodpasture's



### HLA-DR3

- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

### HLA-DR4

- type 1 diabetes mellitus\*
- rheumatoid arthritis

\*type 1 diabetes mellitus is associated with HLA-DR3 but is more strongly associated with HLA-DR4.

Patients with deficiencies of which one of the following complement protein(s) are predisposed to immune complex diseases?

<input type="radio"/>	A. C1-INH
<input type="radio"/>	B. C1q, C1rs, C2, C4
<input type="radio"/>	C. C5-9
<input type="radio"/>	D. C3
<input type="radio"/>	E. C3bBb

[Next question](#)

### Complement deficiencies

Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body. Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency

- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)

- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency

- causes recurrent bacterial infections

C5 deficiency

- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency

- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Which of the following conditions is not caused by a trinucleotide repeat expansion?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Fragile X syndrome    |
| <input type="radio"/> | B. Huntington's          |
| <input type="radio"/> | C. Ataxia telangiectasia |
| <input type="radio"/> | D. Myotonic dystrophy    |
| <input type="radio"/> | E. Friedreich's ataxia   |

Next question

### Trinucleotide repeat disorders

Trinucleotide repeat disorders are genetic conditions caused by an abnormal number of repeats (expansions) of a repetitive sequence of three nucleotides. These expansions are unstable and may enlarge which may lead to an earlier age of onset in successive generations - a phenomenon known as anticipation\*. In most cases, an increase in the severity of symptoms is also noted

Examples - note dominance of neurological disorders

- Fragile X (CGG)
- Huntington's (CAG)
- myotonic dystrophy (CTG)
- Friedreich's ataxia\* (GAA)
- spinocerebellar ataxia
- spinobulbar muscular atrophy
- dentatorubral pallidoluysian atrophy

\*Friedreich's ataxia is unusual in not demonstrating anticipation

Each one of the following causes of hyponatraemia is associated with a urinary sodium of less than 20 mmol/L, except:

<input type="radio"/>	A. Diarrhoea
<input type="radio"/>	B. Psychogenic polydipsia
<input type="radio"/>	C. Burns
<input type="radio"/>	D. Secondary hyperaldosteronism
<input type="radio"/>	E. Syndrome of inappropriate ADH

[Next question](#)

Syndrome of inappropriate ADH is associated with urinary sodium > 20 mmol/l

## Hyponatraemia

Hyponatraemia may be caused by water excess or sodium depletion. Causes of pseudohyponatraemia include hyperlipidaemia (increase in serum volume) or a taking blood from a drip arm. Urinary sodium and osmolality levels aid making a diagnosis

### Urinary sodium > 20 mmol/l

Sodium depletion, renal loss (patient often hypovolaemic)

- diuretics
- Addison's
- diuretic stage of renal failure

Patient often euvolaemic

- SIADH (urine osmolality > 500 mmol/kg)
- hypothyroidism

### Urinary sodium < 20 mmol/l

Sodium depletion, extra-renal loss

- diarrhoea, vomiting, sweating
- burns, adenoma of rectum

Water excess (patient often hypervolaemic and oedematous)

- secondary hyperaldosteronism: CCF, cirrhosis
- reduced GFR: renal failure
- IV dextrose, psychogenic polydipsia

A study is designed to assess the efficacy of a new anti-hypertensive medication. Two groups of patients are randomly assigned, one to take the established drug for 3 months whilst the other takes the new drug for 3 months. Blood pressure is measured before and after the intervention. There is then a period off medication for 1 month. After this period has elapsed the medication that the groups receive is swapped around and again blood pressure is measured before and 3 months later. The difference in blood pressure after the respective medications is calculated for each patient. Which one of the following significance tests is it most appropriate to apply?

<input type="radio"/>	A. Student's unpaired t-test
<input checked="" type="radio"/>	B. Student's paired t-test
<input type="radio"/>	C. Pearson's test
<input type="radio"/>	D. Mann-Whitney test
<input type="radio"/>	E. Chi-squared test

[Next question](#)

This describes a crossover study. As we are comparing parametric data from the same patients (they swapped medication halfway through the study) the Student's paired t-test should be used.

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Which one of the following is the most common genetic cause of Prader-Willi syndrome?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Microdeletion of the paternal 15q11-13       |
| <input type="radio"/> | B. Maternal uniparental disomy of chromosome 15 |
| <input type="radio"/> | C. Paternal uniparental disomy of chromosome 15 |
| <input type="radio"/> | D. Microdeletion of the maternal 15q11-13       |
| <input type="radio"/> | E. Trisomy 18                                   |

Next question

Deletion of chromosome 15

- Prader-Willi - **p**aternal
- Angel**m**an syndrome - **m**aternal

### Prader-Willi syndrome

Prader-Willi syndrome is an example of genetic imprinting where the phenotype depends on whether the deletion occurs on a gene inherited from the mother or father:

- Prader-Willi syndrome if gene deleted from father
- Angelman syndrome if gene deleted from mother

Prader-Willi syndrome is associated with the absence of the active Prader-Willi gene on the long arm of chromosome 15. This may be due to:

- microdeletion of paternal 15q11-13 (70% of cases)
- maternal uniparental disomy of chromosome 15

### Features

- hypotonia during infancy
- dysmorphic features
- short stature
- hypogonadism and infertility
- learning difficulties
- childhood obesity
- behavioural problems in adolescence

A middle-aged man is diagnosed with nasopharyngeal carcinoma. What type of virus family is associated with this malignancy?

<input type="radio"/>	A. Reovirus
<input type="radio"/>	B. Herpesvirus
<input type="radio"/>	C. Parvovirus
<input type="radio"/>	D. Adenovirus
<input type="radio"/>	E. Hepadnaviridae

[Next question](#)

The Epstein-Barr virus is one of the herpes viruses.

#### Epstein-Barr virus: associated conditions

Malignancies associated with EBV infection

- Burkitt's lymphoma\*
- Hodgkin's lymphoma
- nasopharyngeal carcinoma
- HIV-associated central nervous system lymphomas

The non-malignant condition hairy leukoplakia is also associated with EBV infection.

\*EBV is currently thought to be associated with both African and sporadic Burkitt's

### Question 356 of 402

Next

A new biochemical marker has been found which is increased in mothers who are carrying fetuses with Down's syndrome. The new blood test is trialled in 1,000 women over the age of 35 years. Of these women 20 were found to be carrying a fetus with Down's syndrome as assessed using standard measures. The new test was positive in 15 of the 20 cases but was also positive in 30 of the remaining 980 women. What is the positive predictive value of the test?

- ☐ A. 0.66
- ☐ B. 950/980
- ☐ C. 0.33
- ☐ D. 0.8
- ☐ E. 0.5

Next question

A contingency table can be constructed from the above data, as shown below:

	Down's	Not Down's
Test positive	15	30
Test negative	5	950

Positive predictive value =  $TP / (TP + FP) = 15 / (15 + 30) = 0.33$

### Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	$TP / (TP + FN)$	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	$TN / (TN + FP)$	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	$TP / (TP + FP)$	The chance that the patient has the condition if the diagnostic test is positive



<b>Negative predictive value</b>	$TN / (TN + FN)$	The chance that the patient does not have the condition if the diagnostic test is negative
<b>Likelihood ratio for a positive test result</b>	$\text{sensitivity} / (1 - \text{specificity})$	How much the odds of the disease increase when a test is positive
<b>Likelihood ratio for a negative test result</b>	$(1 - \text{sensitivity}) / \text{specificity}$	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

Each one of the following statements regarding atrial natriuretic peptide are true, except:

<input type="radio"/>	A. Lowers blood pressure
<input type="radio"/>	B. Degraded by endopeptidases
<input type="radio"/>	C. Promotes excretion of sodium
<input type="radio"/>	D. Secreted mainly by the left atrium
<input type="radio"/>	E. Antagonises actions of angiotensin II and aldosterone

Next question

## Atrial natriuretic peptide

### Basics

- secreted mainly from myocytes of right atrium and ventricle in response to increased blood volume
- secreted by both the right and left atria (right >> left)
- 28 amino acid peptide hormone, which acts via cGMP
- degraded by endopeptidases

### Actions

- natriuretic, i.e. promotes excretion of sodium
- lowers BP
- antagonises actions of angiotensin II, aldosterone

Which of the following physiological effects would be expected following administration of atropine?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Bradycardia + mydriasis  |
| <input type="radio"/> | B. Tachycardia + miosis     |
| <input type="radio"/> | C. Bradycardia + salivation |
| <input type="radio"/> | D. Bradycardia + miosis     |
| <input type="radio"/> | E. Tachycardia + mydriasis  |

Next question

## Atropine

Atropine is an antagonist of the muscarinic acetylcholine receptor

Uses\*

- treatment of organophosphate poisoning

Physiological effects

- tachycardia
- mydriasis

\*atropine is no longer used in resuscitation

**Question 359 of 402**

Next

You are a ST1 doctor working on a medical ward. You are struggling to cope with the workload and often leave the ward late. Who is the most appropriate action to take?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Take time off-sick until the situation is sorted to protect patient care |
| <input type="radio"/> | B. Speak to the medical director  |
| <input type="radio"/> | C. Arrive one-hour early every morning to give yourself extra time          |
| <input type="radio"/> | D. Speak to your consultant   |
| <input type="radio"/> | E. Speak to the postgraduate dean   |

Next question

Speaking to your consultant is the first action to take in this scenario. They are best placed to be able to take action to try and amend the situation. As the consultant is ultimately responsible for patient care they also have a right to know if you are struggling to cope as this may affect patient care.

The medical director may also be able to assist but would end up speaking to the consultant and hence is not the first choice.

Arriving early may seem an option but does not ultimately address the cause of the problem. Taking time off sick is the worst option - it doesn't address the problem and is unprofessional.

Which one of the following conditions is NOT an autosomal dominant condition?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Retinoblastoma     |
| <input type="radio"/> | B. Tuberose sclerosis |
| <input type="radio"/> | C. Achondroplasia     |
| <input type="radio"/> | D. Myotonic dystrophy |
| <input type="radio"/> | E. Albinism           |

Next question

Autosomal recessive conditions are 'metabolic' - exceptions: inherited ataxias

Autosomal dominant conditions are 'structural' - exceptions: hyperlipidaemia type II, hypokalaemic periodic paralysis

### Autosomal dominant conditions

Autosomal recessive conditions are often thought to be 'metabolic' as opposed to autosomal dominant conditions being 'structural', notable exceptions:

- some 'metabolic' conditions such as Hunter's and G6PD are X-linked recessive whilst others such as hyperlipidaemia type II and hypokalaemic periodic paralysis are autosomal dominant
- some 'structural' conditions such as ataxia telangiectasia and Friedreich's ataxia are autosomal recessive

The following conditions are autosomal dominant:

- Achondroplasia
- Acute intermittent porphyria
- Adult polycystic disease
- Antithrombin III deficiency
- Ehlers-Danlos syndrome
- Familial adenomatous polyposis
- Hereditary haemorrhagic telangiectasia
- Hereditary spherocytosis
- Hereditary non-polyposis colorectal carcinoma
- Huntington's disease
- Hyperlipidaemia type II
- Hypokalaemic periodic paralysis
- Malignant hyperthermia
- Marfan's syndromes

- Myotonic dystrophy
- Neurofibromatosis
- Noonan syndrome
- Osteogenesis imperfecta
- Peutz-Jeghers syndrome
- Retinoblastoma
- Romano-Ward syndrome
- Tuberose sclerosis
- Von Hippel-Lindau syndrome
- Von Willebrand's disease\*

\*type 3 von Willebrand's disease (most severe form) is inherited as an autosomal recessive trait. Around 80% of patients have type 1 disease

Which one of the following causes of primary immunodeficiency is due to a defect in B-cell function?

<input type="radio"/>	A. Di George syndrome
<input type="radio"/>	B. Chediak-Higashi syndrome
<input type="radio"/>	C. Common variable immunodeficiency
<input type="radio"/>	D. Chronic granulomatous disease
<input type="radio"/>	E. Wiskott-Aldrich syndrome

Next question

### Primary immunodeficiency

Primary immunodeficiency disorders may be classified according to which component of the immune system they affect

#### Neutrophil disorders

- chronic granulomatous disease
- Chediak-Higashi syndrome
- leukocyte adhesion deficiency

#### B-cell disorders

- common variable immunodeficiency
- Bruton's congenital agammaglobulinaemia
- IgA deficiency

#### T-cell disorders

- DiGeorge syndrome

#### Combined B- and T-cell disorders

- severe combined immunodeficiency
- ataxic telangiectasia
- Wiskott-Aldrich syndrome

Which of the following is most likely to cause hypokalaemia associated with alkalosis?

<input type="radio"/>	A. Acetazolamide
<input type="radio"/>	B. Partially treated diabetic ketoacidosis
<input type="radio"/>	C. Diarrhoea
<input type="radio"/>	D. Cushing's syndrome
<input type="radio"/>	E. Renal tubular acidosis

Next question

### Hypokalaemia and acid-base balance

Potassium and hydrogen can be thought of as competitors. Hyperkalaemia tends to be associated with acidosis because as potassium levels rise fewer hydrogen ions can enter the cells

Hypokalaemia with alkalosis

- vomiting
- diuretics
- Cushing's syndrome
- Conn's syndrome (primary hyperaldosteronism)

Hypokalaemia with acidosis

- diarrhoea
- renal tubular acidosis
- acetazolamide
- partially treated diabetic ketoacidosis



Which one of the following statements is true regarding cytoplasmic anti-neutrophil cytoplasmic antibodies (cANCA)?

<input type="radio"/>	A. Targeted against myeloperoxidase
<input type="radio"/>	B. Associated with Wegener's granulomatosis
<input type="radio"/>	C. Can be used to monitor activity in autoimmune haemolytic anaemia
<input type="radio"/>	D. Is more commonly seen in ulcerative colitis than perinuclear ANCA
<input type="radio"/>	E. Positive in > 90% of hepatitis C associated vasculitis

Next question

cANCA = Wegener's; pANCA = Churg-Strauss + others

## ANCA

There are two main types of anti-neutrophil cytoplasmic antibodies (ANCA) - cytoplasmic (cANCA) and perinuclear (pANCA)

For the exam, remember:

- cANCA - Wegener's granulomatosis
- pANCA - Churg-Strauss syndrome + others (see below)

### cANCA

- most common target serine proteinase 3 (PR3)
- some correlation between cANCA levels and disease activity
- Wegener's granulomatosis, positive in > 90%
- microscopic polyangiitis, positive in 40%

### pANCA

- most common target is myeloperoxidase (MPO)
- cannot use level of pANCA to monitor disease activity
- associated with immune crescentic glomerulonephritis (positive in c. 80% of patients)
- microscopic polyangiitis, positive in 50-75%
- Churg-Strauss syndrome, positive in 60%
- primary sclerosing cholangitis, positive in 60-80%

- Wegener's granulomatosis, positive in 25%

Other causes of positive ANCA (usually pANCA)

- inflammatory bowel disease (UC > Crohn's)
- connective tissue disorders: RA, SLE, Sjogren's
- autoimmune hepatitis

Which one of the following is most commonly secreted by T-helper cells subset 2 (Th2 cells) ?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Interleukin 2          |
| <input type="radio"/> | B. Tumour necrosis factor |
| <input type="radio"/> | C. Interferon gamma       |
| <input type="radio"/> | D. Interleukin 4          |
| <input type="radio"/> | E. Interleukin 3          |

Next question

### T-Helper cells

There are two major subsets of T-Helper cells:

#### Th1

- involved in the cell mediated response and delayed (type IV) hypersensitivity
- secrete IFN-gamma, IL-2, IL-3

#### Th2

- involved in mediating humoral (antibody) immunity
- e.g. stimulating production of IgE in asthma
- secrete IL-4, IL-5, IL-6, IL-10, IL-13

What is the correct formula to calculate the negative predictive value of a screening test?

TP = true positive; FP = false positive; TN = true negative; FN = false negative

- ☐ A.  $TN / (TN + FN)$
- ☐ B.  $TP / (TP + FP)$
- ☐ C.  $TN / (TN + FP)$
- ☐ D.  $\text{Sensitivity} / (1 - \text{specificity})$
- ☐ E.  $TP / (TP + FN)$

[Next question](#)

### Screening test statistics

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	$TP / (TP + FN)$	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	$TN / (TN + FP)$	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	$TP / (TP + FP)$	The chance that the patient has the condition if the diagnostic test is positive
<b>Negative predictive value</b>	$TN / (TN + FN)$	The chance that the patient does not have the condition if the diagnostic test is negative
<b>Likelihood ratio for a positive test result</b>	$\text{sensitivity} / (1 - \text{specificity})$	How much the odds of the disease increase when a test is positive
<b>Likelihood ratio for a negative test result</b>	$(1 - \text{sensitivity}) / \text{specificity}$	How much the odds of the disease decrease when a test is negative

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent

A study looks at the use of amoxicillin in the treatment of acute sinusitis compared to placebo. The following results are obtained:

	Total number of patients	Number who achieved resolution of symptoms at 7 days
Amoxicillin	100	60
Placebo	75	30

What is the odds ratio a patient achieving resolution of symptoms at 7 days if they take amoxicillin compared to placebo?

- ☐ A. 1.5
- ☐ B. 0.5
- ☐ C. 2.25
- ☐ D. 0.6
- ☐ E. 1.66

Next question

The odds of symptoms resolution with amoxicillin =  $60 / 40 = 1.5$

The odds of symptoms resolution with placebo =  $30 / 45 = (2/3)$

Therefore the odds ratio =  $1.5 / (2/3) = 2.25$

### Odds and odds ratio

Odds are a ratio of the number of people who incur a particular outcome to the number of people who do not incur the outcome. The odds ratio may be defined as the ratio of the odds of a particular outcome with experimental treatment and that of control.

Odds ratios are the usual reported measure in case-control studies. It approximates to relative risk if the outcome of interest is rare.

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Achieved = 50% pain relief
Paracetamol	60	40
Placebo	90	30

The odds of achieving significant pain relief with paracetamol =  $40 / 20 = 2$

The odds of achieving significant pain relief with placebo =  $30 / 60 = 0.5$

Therefore the odds ratio =  $2 / 0.5 = 4$

Where is somatostatin secreted from?

- ☐ A. D cells in the pancreas
- ☐ B. I cells in upper small intestine
- ☐ C. K cells in upper small intestine
- ☐ D. S cells in upper small intestine
- ☐ E. G cells in stomach

Next question

D cells are also found in the stomach and intestine

### Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
<b>Gastrin</b>	G cells in antrum of the stomach	Distension of stomach, vagus nerves (mediated by gastrin-releasing peptide), luminal peptides/amino acids Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
<b>CCK</b>	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
<b>Secretin</b>	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
<b>VIP</b>	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid secretion
<b>Somatostatin</b>	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production

The fasting glucose for a patient is reported as follows:

Glucose (fasting)	6.3 mmol/l
-------------------	------------

What is the most likely underlying pathophysiological change?

- |                                  |                                      |
|----------------------------------|--------------------------------------|
| <input type="radio"/>            | A. Beta-cell hyperplasia             |
| <input type="radio"/>            | B. Beta-cell atrophy                 |
| <input type="radio"/>            | C. Muscle insulin resistance         |
| <input checked="" type="radio"/> | D. Hepatic insulin resistance        |
| <input type="radio"/>            | E. Adipose tissue insulin resistance |

Next question

### Impaired glucose regulation

Impaired glucose regulation (IGR) may also be referred to as non-diabetic hyperglycaemia (NDH) or prediabetes. It describes blood glucose levels which are above the normal range but not high enough for a diagnosis of diabetes mellitus. Diabetes UK estimate that around 1 in 7 adults in the UK have IGR. Many individuals with IGR will progress on to developing type 2 diabetes mellitus (T2DM) and they are therefore at greater risk of microvascular and macrovascular complications.

There are two main types of IGR:

- impaired fasting glucose (IFG) - due to hepatic insulin resistance
- impaired glucose tolerance (IGT) - due to muscle insulin resistance
- patients with IGT are more likely to develop T2DM and cardiovascular disease than patients with IFG

### Definitions

- a fasting glucose greater than or equal to 6.1 but less than 7.0 mmol/l implies impaired fasting glucose (IFG)
- impaired glucose tolerance (IGT) is defined as fasting plasma glucose less than 7.0 mmol/l and OGTT 2-hour value greater than or equal to 7.8 mmol/l but less than 11.1 mmol/l
- the role of HbA1c in diagnosing IGR and diabetes is currently under review
- people with IFG should then be offered an oral glucose tolerance test to rule out a diagnosis of diabetes. A result below 11.1 mmol/l but above 7.8 mmol/l indicates that the person doesn't have diabetes but does have IGT

## Management

- Diabetes UK suggests using the term 'prediabetes' when discussing the condition with patients as research has shown that this term has the most impact and is most easily understood
- lifestyle modification: weight loss, increased exercise, change in diet
- drug therapy is not currently licensed or recommended for patients with IGR in the UK
- at least yearly follow-up with blood tests is recommended



A 23-year-old man is admitted with sepsis. Blood cultures are reported as follows:

*Neisseria gonorrhoeae*

Which of the following complement proteins is the patient most likely to deficient in?

<input type="radio"/>	A. C1q, C1rs, C2, C4
<input type="radio"/>	B. C3a + C5a
<input type="radio"/>	C. C5-9
<input type="radio"/>	D. C4
<input type="radio"/>	E. C2

Whilst C3 deficiency is associated with recurrent bacterial infections, C5 deficiency is more characteristically associated with disseminated meningococcal infection and other Gram negative diplococcal infections

### Complement deficiencies

Complement is a series of proteins that circulate in plasma and are involved in the inflammatory and immune reaction of the body. Complement proteins are involved in chemotaxis, cell lysis and opsonisation

C1 inhibitor (C1-INH) protein deficiency

- causes hereditary angioedema
- C1-INH is a multifunctional serine protease inhibitor
- probable mechanism is uncontrolled release of bradykinin resulting in oedema of tissues

C1q, C1rs, C2, C4 deficiency (classical pathway components)

- predisposes to immune complex disease
- e.g. SLE, Henoch-Schonlein Purpura

C3 deficiency

- causes recurrent bacterial infections

C5 deficiency

- predisposes to Leiner disease
- recurrent diarrhoea, wasting and seborrhoeic dermatitis

C5-9 deficiency

- encodes the membrane attack complex (MAC)
- particularly prone to *Neisseria meningitidis* infection

Which one of the following is least associated with Reye's syndrome?

<input type="radio"/>	A. Hypoglycaemia
<input type="radio"/>	B. Preceding aspirin use
<input type="radio"/>	C. Purpuric skin lesions
<input type="radio"/>	D. Seizures
<input type="radio"/>	E. Preceding viral infection

Next question

#### Reye's syndrome

- viral/aspirin use may trigger
- features include encephalopathy, fatty infiltration and hypoglycaemia

#### Reye's syndrome

Reye's syndrome is a severe, progressive encephalopathy affecting children that is accompanied by fatty infiltration of the liver, kidneys and pancreas. The aetiology of Reye's syndrome is not fully understood although there is a known association with aspirin use and a viral cause has been postulated

The peak incidence is 2 years of age, features include:

- may be history of preceding viral illness
- encephalopathy: confusion, seizures, cerebral oedema, coma
- fatty infiltration of the liver, kidneys and pancreas
- hypoglycaemia

Management is supportive

Although the prognosis has improved over recent years there is still a mortality rate of 15-25%.

A 16-year-old male is reviewed in the endocrinology clinic due to lack of pubertal development. On examination his testes are undescended and there is only scanty pubic hair. What is the most likely diagnosis?

<input type="radio"/>	A. Down's syndrome
<input checked="" type="radio"/>	B. Kallman's syndrome
<input type="radio"/>	C. Dubin-Johnson syndrome
<input type="radio"/>	D. Turner's syndrome
<input type="radio"/>	E. Klinefelter's syndrome

[Next question](#)

Cryptorchidism is more suggestive of Kallman's than Klinefelter's syndrome

### Kallman's syndrome

Kallman's syndrome is a recognised cause of delayed puberty secondary to hypogonadotrophic hypogonadism. It is usually inherited as an X-linked recessive trait. Kallman's syndrome is thought to be caused by failure of GnRH-secreting neurons to migrate to the hypothalamus.

The clue given in many questions is lack of smell (anosmia) in a boy with delayed puberty

### Features

- 'delayed puberty'
- hypogonadism, cryptorchidism
- anosmia
- sex hormone levels are low
- LH, FSH levels are inappropriately low/normal
- patients are typically of normal or above average height

Cleft lip/palate and visual/hearing defects are also seen in some patients

Which one of the following statements regarding significance tests is incorrect?

<input type="radio"/>	A. Parametric data is usually normally distributed
<input type="radio"/>	B. Student's t-test may be paired on unpaired
<input type="radio"/>	C. Pearson's product-moment coefficient is used to assess correlation between two variables
<input type="radio"/>	D. Chi-squared test is used to compare parametric data
<input type="radio"/>	E. Paired data refers to data obtained from a single group of patients

Next question

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

Which cell organelle is involved in the synthesis of lipids?

- ☐ A. Golgi apparatus
- ☐ B. Smooth endoplasmic reticulum
- ☐ C. Ribosome
- ☐ D. Rough endoplasmic reticulum
- ☐ E. Nucleolus

[Next question](#)

## Cell organelles

The table below summarises the main functions of the major cell organelles:

Organelle/macromolecule	Main function
Endoplasmic reticulum	Translation and folding of new proteins (rough endoplasmic reticulum), expression of lipids (smooth endoplasmic reticulum)
Golgi apparatus	Sorting and modification of proteins
Mitochondrion	Aerobic respiration. Contains mitochondrial genome as circular DNA
Nucleus	DNA maintenance and RNA transcription
Lysosome	Breakdown of large molecules such as proteins and polysaccharides
Nucleolus	Ribosome production
Ribosome	Translation of RNA into proteins
Peroxisome	Breakdown of metabolic hydrogen peroxide
Proteasome	Along with lysosome pathway involved in degradation of large protein molecules

Which one of the following features is least associated with zinc deficiency?

<input type="radio"/>	A. Acrodermatitis
<input type="radio"/>	B. Alopecia
<input type="radio"/>	C. Short stature
<input type="radio"/>	D. Perioral dermatitis
<input type="radio"/>	E. Gingivitis

Next question

Gingivitis is more commonly seen in vitamin C deficiency

### Zinc deficiency

#### Features

- perioral dermatitis: red, crusted lesions
- acrodermatitis
- alopecia
- short stature
- hypogonadism
- hepatosplenomegaly
- geophagia (ingesting clay/soil)
- cognitive impairment

Which one of the following features is most likely to be seen following facial nerve paralysis?

<input type="radio"/>	A. Hyperacusis
<input type="radio"/>	B. Hyperlacrimation
<input type="radio"/>	C. Hyperesthesia
<input type="radio"/>	D. Hyperalgesia
<input type="radio"/>	E. Hypersalivation

Hyperacusis results from paralysis of the stapedius muscle. Overflow of tears may occur but hyperlacrimation does not.

### Facial nerve

Supply - 'face, ear, taste, tear'

- face: muscles of facial expression
- ear: nerve to stapedius
- taste: supplies anterior two-thirds of tongue
- tear: parasympathetic fibres to lacrimal glands, also salivary glands

Causes of bilateral facial nerve palsy

- sarcoidosis
- Guillain-Barre syndrome
- polio, Lyme disease

Causes of unilateral facial nerve palsy - as above plus

Lower motor neuron	Upper motor neuron
<ul style="list-style-type: none"> <li>• Bell's palsy</li> <li>• Ramsay-Hunt syndrome (due to herpes zoster)</li> <li>• acoustic neuroma</li> <li>• parotid tumours</li> <li>• HIV</li> <li>• multiple sclerosis*</li> <li>• diabetes mellitus</li> </ul>	<ul style="list-style-type: none"> <li>• stroke</li> </ul>

LMN vs. UMN

- upper motor neuron lesion 'spares' upper face i.e. forehead
- lower motor neuron lesion affects all facial muscles

\*may also cause an UMN palsy

Which one of the following hormones is most responsible for the secretion of bicarbonate in the upper gastrointestinal tract?

- ☐ A. Somatostatin
- ☐ B. Gastrin
- ☐ C. Secretin
- ☐ D. CCK
- ☐ E. Vasoactive intestinal peptide

[Next question](#)

### Gastrointestinal hormones

Below is a brief summary of the major hormones involved in food digestion:

	Source	Stimulus	Actions
<b>Gastrin</b>	G cells in antrum of the stomach	Distension of stomach, vagus nerves (mediated by gastrin-releasing peptide), luminal peptides/amino acids Inhibited by: low antral pH, somatostatin	Increase HCL, pepsinogen and IF secretion, increases gastric motility, trophic effect on gastric mucosa
<b>CCK</b>	I cells in upper small intestine	Partially digested proteins and triglycerides	Increases secretion of enzyme-rich fluid from pancreas, contraction of gallbladder and relaxation of sphincter of Oddi, decreases gastric emptying, trophic effect on pancreatic acinar cells, induces satiety
<b>Secretin</b>	S cells in upper small intestine	Acidic chyme, fatty acids	Increases secretion of bicarbonate-rich fluid from pancreas and hepatic duct cells, decreases gastric acid secretion, trophic effect on pancreatic acinar cells
<b>VIP</b>	Small intestine, pancreas	Neural	Stimulates secretion by pancreas and intestines, inhibits acid secretion
<b>Somatostatin</b>	D cells in the pancreas & stomach	Fat, bile salts and glucose in the intestinal lumen	Decreases acid and pepsin secretion, decreases gastrin secretion, decreases pancreatic enzyme secretion, decreases insulin and glucagon secretion inhibits trophic effects of gastrin, stimulates gastric mucous production



Which one of the following syndromes is associated with an increased risk of Crohn's disease?

<input type="radio"/>	A. Turner's syndrome
<input type="radio"/>	B. Down's syndrome
<input type="radio"/>	C. Fragile X syndrome
<input type="radio"/>	D. Patau syndrome
<input type="radio"/>	E. Edward's syndrome

Next question

### Turner's syndrome

Turner's syndrome is a chromosomal disorder affecting around 1 in 2,500 females. It is caused by either the presence of only one sex chromosome (X) or a deletion of the short arm of one of the X chromosomes. Turner's syndrome is denoted as 45,XO or 45,X

#### Features

- short stature
- shield chest, widely spaced nipples
- webbed neck
- bicuspid aortic valve (15%), coarctation of the aorta (5-10%)
- primary amenorrhoea
- high-arched palate
- short fourth metacarpal
- multiple pigmented naevi
- lymphoedema in neonates (especially feet)

There is also an increased incidence of autoimmune disease (especially autoimmune thyroiditis) and Crohn's disease

Which layer of the epidermis is immediately next to the dermis?

- ☐ A. Stratum granulosum
- ☐ B. Stratum lucidum
- ☐ C. Stratum corneum
- ☐ D. Stratum germinativum
- ☐ E. Stratum spinosum

Next question

Epidermis - 5 layers - bottom layer = stratum germinativum which gives rise to keratinocytes and contains melanocytes

## Epidermis

The epidermis is the outermost layer of the skin and is composed of a stratified squamous epithelium with an underlying basal lamina

It may be divided in to five layers:

Layer	Description
Stratum corneum	Flat, dead, scale-like cells filled with keratin Continually shed
Stratum lucidum	Clear layer - present in thick skin only
Stratum granulosum	Cells form links with neighbours
Stratum spinosum	Squamous cells begin keratin synthesis Thickest layer of epidermis
Stratum germinativum	The basement membrane - single layer of columnar epithelial cells Gives rise to keratinocytes Contains melanocytes

A mutation in the gene that encodes aquaporin 2 is most likely to result in:

<input type="radio"/>	A. Histiocytosis
<input type="radio"/>	B. Alport's syndrome
<input type="radio"/>	C. Minimal change disease
<input type="radio"/>	D. Diabetes insipidus
<input type="radio"/>	E. Medullary sponge kidney

[Next question](#)

### Diabetes insipidus

Diabetes insipidus (DI) is a condition characterised by either a deficiency of antidiuretic hormone, ADH, (cranial DI) or an insensitivity to antidiuretic hormone (nephrogenic DI).

#### Causes of cranial DI

- idiopathic
- post head injury
- pituitary surgery
- craniopharyngiomas
- histiocytosis X
- DIDMOAD is the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

#### Causes of nephrogenic DI

- genetic: the more common form affects the vasopressin (ADH) receptor, the less common form results from a mutation in the gene that encodes the aquaporin 2 channel
- electrolytes: hypercalcaemia, hypokalaemia
- drugs: demeclocycline, lithium
- tubulo-interstitial disease: obstruction, sickle-cell, pyelonephritis

#### Features

- polyuria
- polydipsia

#### Investigation

- high plasma osmolarity, low urine osmolarity
- water deprivation test

The adrenergic receptor is an example of a:

<input type="radio"/>	A. Intracellular receptor
<input type="radio"/>	B. Tyrosine kinase receptor
<input type="radio"/>	C. Guanylate cyclase receptor
<input type="radio"/>	D. G protein-coupled receptor
<input type="radio"/>	E. Ligand-gated ion channel

Next question

## Membrane receptors

There are four main types of membrane receptor: ligand-gated ion channels, tyrosine kinase receptors, guanylate cyclase receptors and G protein-coupled receptors

Ligand-gated ion channel

- generally mediate fast responses
- e.g. nicotinic acetylcholine, GABA-A & GABA-C, glutamate receptors

Tyrosine kinase receptors

- contain intrinsic enzyme activity
- e.g. insulin, growth factors, interferon

Guanylate cyclase receptors

- contain intrinsic enzyme activity
- e.g. atrial natriuretic factor receptors

G protein-coupled receptors

- generally mediate slow transmission and affect metabolic processes
- activated by a wide variety of extracellular signals e.g. Peptide hormones, biogenic amines, lipophilic hormones, light
- consist of 3 main subunits: alpha, beta and gamma
- ligand binding causes conformational changes to receptor, this induces exchange of GDP for GTP
- e.g. Muscarinic acetylcholine, adrenergic receptors, GABA-B

A study is performed comparing two chemotherapy regimes for patients with small cell lung cancer. The end point of the study is survival time. Which one of the following types statistical measures is it most appropriate to compare survival time with?

<input type="radio"/>	A. Odds ratio
<input type="radio"/>	B. Pearson's product-moment coefficient
<input type="radio"/>	C. Relative risk
<input type="radio"/>	D. Hazard ratio
<input type="radio"/>	E. Absolute risk reduction

[Next question](#)

### Hazard ratio

The hazard ratio (HR) is similar to relative risk but is used when risk is not constant to time. It is typically used when analysing survival over time

You are caring for a local cardiology consultant's father who has been admitted following a myocardial infarction. He bleeps you from the switchboard and asks how his father is doing. You recognise his voice on the phone. What is the most appropriate response?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Decline to give any details over the phone but offer to meet the consultant face-to-face for a chat |
| <input type="radio"/> | B. As a matter of professional courtesy ask for his advice on post-myocardial infarction care          |
| <input type="radio"/> | C. Ask permission from his father then give relevant details   |
| <input type="radio"/> | D. Give full details include the troponin I value and offer to fax the ECG                             |
| <input type="radio"/> | E. Say he is 'doing fine'  |

Next question

The main nub of this question relates to confidentiality. You cannot give details over the phone to anyone, even his son, without the patient's express permission. Whilst it may be presumed that this is what the patient would want it is impossible to be sure of the family dynamics.

If the patient has given permission and you are sure you are speaking to the son then giving relevant details is the best option. Asking the consultant to come in as an option but may not be necessary if the previous conditions are met. Saying he is 'doing fine' is unlikely to satisfy a consultant cardiologist.

Giving details without first getting permission from the patient is breaking confidentiality, however well intentioned. Involving a relative in the management of a patient is inappropriate and the worst option.

**Question 383 of 402**

Next

A contingency table is constructed for a new blood protein marker to screen for prostate cancer in men aged between 50 and 70 years:

	Prostate cancer present	Prostate cancer absent
New test positive	19	20
New test negative	14	723

What is the positive predictive value of the new test?

- ☐ A. 19/20
- ☐ B. 723/743
- ☐ C. 19/39
- ☐ D. 19/33
- ☐ E. 723/737

Next question

Positive predictive value = true positives / (true positives + false positives)

$$= 19 / (19 + 20)$$

**Screening test statistics**

It would be unusual for a medical exam not to feature a question based around screening test statistics. The available data should be used to construct a contingency table as below:

TP = true positive; FP = false positive; TN = true negative; FN = false negative

	Disease present	Disease absent
Test positive	TP	FP
Test negative	FN	TN

The table below lists the main statistical terms used in relation to screening tests:

<b>Sensitivity</b>	TP / (TP + FN )	Proportion of patients with the condition who have a positive test result
<b>Specificity</b>	TN / (TN + FP)	Proportion of patients without the condition who have a negative test result
<b>Positive predictive value</b>	TP / (TP + FP)	The chance that the patient has the condition if the diagnostic test is positive
<b>Negative predictive value</b>	TN / (TN + FN)	The chance that the patient does not have the condition if the diagnostic test is negative
<b>Likelihood ratio for a positive test result</b>	sensitivity / (1 - specificity)	How much the odds of the disease increase when a test is positive

<b>Likelihood ratio for a negative test result</b>	$(1 - \text{sensitivity}) / \text{specificity}$	How much the odds of the disease decrease when a test is negative
--	---	---

Positive and negative predictive values are prevalence dependent. Likelihood ratios are not prevalence dependent



A 45-year-old man who is known to have Marfan's syndrome presents with lower back pain. This has been present for a few months now and is associated with headaches, leg pain and intermittent episodes of urinary incontinence. What is the most likely diagnosis?

<input type="radio"/>	A. Depression
<input type="radio"/>	B. Spinal stenosis
<input type="radio"/>	C. Leaking aortic abdominal aneurysm
<input type="radio"/>	D. Multiple sclerosis
<input type="radio"/>	E. Dural ectasia

[Next question](#)

Dural ectasia affects around 60% of patients with Marfan's syndrome. It may cause lower back pain associated with neurological problems such as bladder and bowel dysfunction.

### Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 people.

#### Features

- tall stature with arm span to height ratio  $> 1.05$
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of  $> 20$  degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.

Pellagra is caused by a deficiency in:

- |                       |                   |
|-----------------------|-------------------|
| <input type="radio"/> | A. Vitamin B12    |
| <input type="radio"/> | B. Thiamine       |
| <input type="radio"/> | C. Nicotinic acid |
| <input type="radio"/> | D. Vitamin B2     |
| <input type="radio"/> | E. Vitamin B6     |

Next question

## Pellagra

Pellagra is caused by nicotinic acid (niacin) deficiency. The classical features are the 3 D's - dermatitis, diarrhoea and dementia

Pellagra may occur as a consequence of isoniazid therapy (isoniazid inhibits the conversion of tryptophan to niacin) and it is more common in alcoholics.

### Features

- dermatitis (brown scaly rash on sun-exposed sites - termed Casal's necklace if around neck)
- diarrhoea
- dementia, depression
- death if not treated

A 62-year-old man is admitted to resus with a low GCS. Blood gases taken on admission show the following:

pH	7.23
pCO <sub>2</sub>	2.2 kPa
pO <sub>2</sub>	13.8 kPa

IV access is obtained and bloods are taken. He is given supportive care with oxygen and fluids. Renal function results show:

Na <sup>+</sup>	143 mmol/l
K <sup>+</sup>	4.2 mmol/l
Chloride	109 mmol/l
Bicarbonate	12 mmol/l
Urea	2.1 mmol/l
Creatinine	79 µmol/l
Glucose	7.1 mmol/l

Which one of the following diagnoses would be most consistent with these results?

- ☐ A. Massive pulmonary embolism
- ☐ B. Methanol poisoning
- ☐ C. Paraquat poisoning
- ☐ D. Diabetic ketoacidosis
- ☐ E. Addisonian crisis

Next question

This patient has a raised anion gap metabolic acidosis which may be caused by methanol poisoning. Massive pulmonary embolism is unlikely given the pO<sub>2</sub> as is diabetic ketoacidosis given the blood glucose.

### Metabolic acidosis

Metabolic acidosis is commonly classified according to the anion gap. This can be calculated by:  $(\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-)$ . If a question supplies the chloride level then this is often a clue that the anion gap should be calculated. The normal range = 10-18 mmol/L

Normal anion gap ( = hyperchloraemic metabolic acidosis)

- gastrointestinal bicarbonate loss: diarrhoea, ureterosigmoidostomy, fistula
- renal tubular acidosis
- drugs: e.g. acetazolamide

- ammonium chloride injection
- Addison's disease

#### Raised anion gap

- lactate: shock, hypoxia
- ketones: diabetic ketoacidosis, alcohol
- urate: renal failure
- acid poisoning: salicylates, methanol

Metabolic acidosis secondary to high lactate levels may be subdivided into two types:

- lactic acidosis type A: shock, hypoxia, burns
- lactic acidosis type B: metformin

Potential complications of Paget's disease include each of the following except:

<input type="radio"/>	A. Deafness
<input type="radio"/>	B. Cerebral calcification
<input type="radio"/>	C. Skull thickening
<input type="radio"/>	D. Bone sarcoma
<input type="radio"/>	E. Fractures

Next question

### Paget's disease of the bone

Paget's disease is a disease of increased but uncontrolled bone turnover. It is thought to be primarily a disorder of osteoclasts, with excessive osteoclastic resorption followed by increased osteoblastic activity. Paget's disease is common (UK prevalence 5%) but symptomatic in only 1 in 20 patients

Predisposing factors

- increasing age
- male sex
- northern latitude
- family history

Clinical features - only 5% of patients are symptomatic

- bone pain (e.g. pelvis, lumbar spine, femur)
- classical, untreated features: bowing of tibia, bossing of skull
- raised alkaline phosphatase (ALP) - calcium\* and phosphate are typically normal
- skull x-ray: thickened vault, osteoporosis circumscripta

Indications for treatment include bone pain, skull or long bone deformity, fracture, periarticular Paget's

- bisphosphonate (either oral risedronate or IV zoledronate)
- calcitonin is less commonly used now

Complications

- deafness (cranial nerve entrapment)
- bone sarcoma (1% if affected for > 10 years)
- fractures
- skull thickening
- high-output cardiac failure

\*usually normal in this condition but hypercalcaemia may occur with prolonged immobilisation

Which one of the following immunoglobulins is involved in the activation of B-cells?

- ☐ A. IgD
- ☐ B. IgM
- ☐ C. IgE
- ☐ D. IgG
- ☐ E. IgA

Next question

IgD is involved in the activation of B-cells

### Immunoglobulins

The table below summarises the characteristics of the 5 types of immunoglobulin found in the body:

<b>IgG</b>	75%	Monomer	Enhance phagocytosis of bacteria and viruses, pass to fetal circulation
<b>IgA</b>	15%	Monomer/ dimer	Found in secretions, provide localized protection on mucous membranes
<b>IgM</b>	10%	Pentamer	first to be secreted, anti-A, B blood antibodies
<b>IgD</b>	1%	Monomer	Involved in activation of B cells
<b>IgE</b>	0.1%	Monomer	Involved in allergic reactions

**Question 389 of 402**

Next

A 25-year-old woman presents with a symmetrical arthropathy affecting her hands. On examination she has synovitis of the 2nd and 3rd metacarpophalangeal joints. What type of HLA allele is most associated with this condition?

- |                       |            |
|-----------------------|------------|
| <input type="radio"/> | A. HLA DR3 |
| <input type="radio"/> | B. HLA A3  |
| <input type="radio"/> | C. HLA DR4 |
| <input type="radio"/> | D. HLA DR2 |
| <input type="radio"/> | E. HLA B27 |

Next question

Rheumatoid arthritis - HLA DR4

This patient has rheumatoid arthritis.

**HLA associations**

HLA antigens are encoded for by genes on chromosome 6. HLA A, B and C are class I antigens whilst DP, DQ, DR are class II antigens. Questions are often based around which diseases have strong HLA associations. The most important associations are listed below:

**HLA-A3**

- haemochromatosis

**HLA-B5**

- Behcet's disease

**HLA-B27**

- ankylosing spondylitis
- Reiter's syndrome
- acute anterior uveitis

**HLA-DQ2/DQ8**

- coeliac disease

## HLA-DR2

- narcolepsy
- Goodpasture's

## HLA-DR3

- dermatitis herpetiformis
- Sjogren's syndrome
- primary biliary cirrhosis

## HLA-DR4

- type 1 diabetes mellitus\*
- rheumatoid arthritis

\*type 1 diabetes mellitus is associated with HLA-DR3 but is more strongly associated with HLA-DR4.



Which one of the following is in direct anatomical contact with the right kidney?

- ☐ A. Gallbladder
- ☐ B. Liver
- ☐ C. Stomach
- ☐ D. Distal part of small intestine
- ☐ E. Duodenum

Next question

## Renal anatomy

The tables below show the anatomical relations of the kidneys:

Right kidney

Direct contact	Layer of peritoneum in-between
Right suprarenal gland	Liver
Duodenum	Distal part of small intestine
Colon	

Left kidney

Direct contact	Layer of peritoneum in-between
Left suprarenal gland	Stomach
Pancreas	Spleen
Colon	Distal part of small intestine

Which of the following is not true regarding B-type natriuretic peptide?

<input type="radio"/>	A. Secreted mainly by the ventricles
<input type="radio"/>	B. Acts as a diuretic
<input type="radio"/>	C. Acts as a vasoconstrictor
<input type="radio"/>	D. Levels rise in left ventricular failure
<input type="radio"/>	E. Reduces sympathetic tone

Next question

BNP - actions:

- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

### B-type natriuretic peptide

B-type natriuretic peptide (BNP) is a hormone produced mainly by the left ventricular myocardium in response to strain.

Whilst heart failure is the most obvious cause of raised BNP levels any cause of left ventricular dysfunction such as myocardial ischaemia or valvular disease may raise levels. Raised levels may also be seen due to reduced excretion in patients with chronic kidney disease. Factors which reduce BNP levels include treatment with ACE inhibitors, angiotensin-2 receptor blockers and diuretics.

Effects of BNP

- vasodilator
- diuretic and natriuretic
- suppresses both sympathetic tone and the renin-angiotensin-aldosterone system

### Clinical uses of BNP

Diagnosing patients with acute dyspnoea

- a low concentration of BNP(< 100pg/ml) makes a diagnosis of heart failure unlikely, but raised levels should prompt further investigation to confirm the diagnosis

- NICE currently recommends BNP as a helpful test to rule out a diagnosis of heart failure

#### Prognosis in patients with chronic heart failure

- initial evidence suggests BNP is an extremely useful marker of prognosis

#### Guiding treatment in patients with chronic heart failure

- effective treatment lowers BNP levels

#### Screening for cardiac dysfunction

- not currently recommended for population screening

You are a ST1 doctor in medicine doing a nightshift. An elderly patient with colorectal cancer has been admitted to the Emergency Department with suspected bowel obstruction. The Emergency Department F2 doctor has tried to refer the patient to the surgeons but was told that as no surgical intervention is likely the patient should be admitted to the medics. The F2 doctor therefore phones yourself and asks you to accept the patient. What is the most appropriate response?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Accept the patient and ask the staff to transfer her to the medical assessment unit                                   |
| <input type="radio"/> | B. Simply refuse in order to avoid the patient being admitted under an inappropriate specialty                           |
| <input type="radio"/> | C. Tell the surgical registrar that you will contact the on-call surgical consultant if he refuses to accept the patient |
| <input type="radio"/> | D. Go down to the emergency department and review the patient  |
| <input type="radio"/> | E. Phone the surgical team yourself to discuss the matter  |

Next question

Scenarios similar to this occur on an almost daily basis for admitting medical teams. The priority in all of this has to be the patient. It may be the case if the patient is end-stage then medical admission is more appropriate. If they are Duke's A and awaiting an operation then clearly they are surgical. Until you review the patient yourself you will not have all the facts and this is therefore the best option.

Discussing the matter with the surgical team will help to clarify their opinion about the patient and is the next best option. Accepting the patient without review risks placing a patient with an acute surgical problem on a medical ward. This may delay or compromise care.

Getting into an argument with the surgical registrar is not constructive and is a poor choice, as is simply refusing to see the patient as this indicates a disregard for the patient.

A new adjuvant treatment for women with breast cancer is investigated. The study looks at the recurrence rate after 5 years. The following data is obtained:

	Number of patients	Number who had a recurrence within a 5 year period
New drug	200	40
Placebo	400	100

What is the relative risk reduction?

- ☐ A. 50%
- ☐ B. 20%
- ☐ C. 4
- ☐ D. 0.8
- ☐ E. 5%

Next question

$$\text{Relative risk reduction} = (\text{EER} - \text{CER}) / \text{CER}$$

Experimental event rate,  $\text{EER} = 40 / 200 = 0.2$

Control event rate,  $\text{CER} = 100 / 400 = 0.25$

Relative risk reduction =  $(\text{EER} - \text{CER}) / \text{CER} = (0.2 - 0.25) / 0.25 = -0.2$  or a 20% reduction

### Relative risk

**Relative risk (RR)** is the ratio of risk in the experimental group (experimental event rate, EER) to risk in the control group (control event rate, CER). The term relative risk ratio is sometimes used instead of relative risk.

To recap

- EER = rate at which events occur in the experimental group
- CER = rate at which events occur in the control group

For example, if we look at a trial comparing the use of paracetamol for dysmenorrhoea compared to placebo we may get the following results

	Total number of patients	Experienced significant pain relief
Paracetamol	100	60

Placebo	80	20
---------	----	----

Experimental event rate,  $EER = 60 / 100 = 0.6$

Control event rate,  $CER = 20 / 80 = 0.25$

Therefore the relative risk ratio =  $EER / CER = 0.6 / 0.25 = 2.4$

If the risk ratio is  $> 1$  then the rate of an event (in this case experiencing significant pain relief) is increased compared to controls. It is therefore appropriate to calculate the relative risk increase if necessary (see below).

If the risk ratio is  $< 1$  then the rate of an event is decreased compared to controls. The relative risk reduction should therefore be calculated (see below).

**Relative risk reduction (RRR)** or **relative risk increase (RRI)** is calculated by dividing the absolute risk change by the control event rate

Using the above data,  $RRI = (EER - CER) / CER = (0.6 - 0.25) / 0.25 = 1.4 = 140\%$

A couple present for genetic counselling. The male partner has haemophilia whilst the female partner has been screened and shown to be a carrier of the gene causing haemophilia. What is the chance that a future child would have haemophilia?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. 25% if male child, 0% if female child  |
| <input type="radio"/> | B. 50%                                    |
| <input type="radio"/> | C. 100% if male child, 0% if female child |
| <input type="radio"/> | D. 50% if male child, 0% if female child  |
| <input type="radio"/> | E. 25%                                    |

[Next question](#)

This question asks about the unusual situation of an affected male having children with a heterozygous (carrier) female. In this situation 50% of all children will be affected

### X-linked recessive

In X-linked recessive inheritance only males are affected. An exception to this seen in examinations are patients with Turner's syndrome, who are affected due to only having one X chromosome. X-linked recessive disorders are transmitted by heterozygote females (carriers) and male-to-male transmission is not seen. Affected males can only have unaffected sons and carrier daughters.

Each male child of a heterozygous female carrier has a 50% chance of being affected whilst each female child of a heterozygous female carrier has a 50% chance of being a carrier.

The possibility of an affected father having children with a heterozygous female carrier is generally speaking extremely rare. However, in certain Afro-Caribbean communities G6PD deficiency is relatively common and homozygous females with clinical manifestations of the enzyme defect are seen.

Which one of the following is not a risk factor for the development of pre-eclampsia?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Body mass index of 38 kg/m <sup>2</sup> |
| <input type="radio"/> | B. Smoking                                 |
| <input type="radio"/> | C. A woman carrying twins                  |
| <input type="radio"/> | D. Nulliparity                             |
| <input type="radio"/> | E. Diabetes mellitus                       |

Next question

There is some evidence to suggest that pre-eclampsia is actually less common in smokers

### Pre-eclampsia

Pre-eclampsia is a condition seen after 20 weeks gestation characterised by pregnancy-induced hypertension in association with proteinuria (> 0.3g / 24 hours). Oedema used to be third element of the classic triad but is now often not included in the definition as it is not specific

Pre-eclampsia is important as it predisposes to the following problems

- fetal: prematurity, intrauterine growth retardation
- eclampsia
- haemorrhage: placental abruption, intra-abdominal, intra-cerebral
- cardiac failure
- multi-organ failure

### Risk factors

- > 40 years old
- nulliparity (or new partner)
- multiple pregnancy
- body mass index > 30 kg/m<sup>2</sup>
- diabetes mellitus
- pregnancy interval of more than 10 years
- family history of pre-eclampsia
- previous history of pre-eclampsia
- pre-existing vascular disease such as hypertension or renal disease

### Features of severe pre-eclampsia

- hypertension: typically > 170/110 mmHg and proteinuria as above
- proteinuria: dipstick ++/+++



- headache
- visual disturbance
- papilloedema
- RUQ/epigastric pain
- hyperreflexia
- platelet count  $< 100 \times 10^6/l$ , abnormal liver enzymes or HELLP syndrome

## Management

- consensus guidelines recommend treating blood pressure  $> 160/110$  mmHg although many clinicians have a lower threshold
- oral labetalol is now first-line following the 2010 NICE guidelines. Nifedipine and hydralazine may also be used
- delivery of the baby is the most important and definitive management step. The timing depends on the individual clinical scenario

The average weight loss of a patient following a new type of bariatric surgery is 18 kg. The standard deviation of weight loss is 3kg. Assuming the weight loss is normally distributed, what percentage of patients will loss between 9 and 27 kg?

<input type="radio"/>	A. 97.4%
<input type="radio"/>	B. 95%
<input type="radio"/>	C. 95.4%
<input type="radio"/>	D. 68.3%
<input type="radio"/>	E. 99.7%

[Next question](#)

99.7% of values of a normally distributed variable lie within 3 standard deviations of the mean.

### Normal distribution

The normal distribution is also known as the Gaussian distribution or 'bell-shaped' distribution. It describes the spread of many biological and clinical measurements

#### Properties of the Normal distribution

- symmetrical i.e. Mean = mode = median
- 68.3% of values lie within 1 SD of the mean
- 95.4% of values lie within 2 SD of the mean
- 99.7% of values lie within 3 SD of the mean
- this is often reversed, so that within 1.96 SD of the mean lie 95% of the sample values
- the range of the mean - (1.96 \*SD) to the mean + (1.96 \* SD) is called the 95% confidence interval, i.e. If a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range

#### Standard deviation

- the standard deviation (SD) is a measure of how much dispersion exists from the mean
- SD = square root (variance)

**Question 397 of 402**

Next

A small study looks at the weight of patients diagnosed with type 2 diabetes mellitus. Overall 64 patients were reviewed. The average weight was 81 kg, with a standard deviation of 12 kg. What is the standard error of the mean?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Square root (64 / 12) |
| <input type="radio"/> | B. Square root (81 / 12) |
| <input type="radio"/> | C. 12 / 9                |
| <input type="radio"/> | D. 9 / 12                |
| <input type="radio"/> | E. 1.5                   |

Next question

Standard error of the mean = standard deviation / square root (number of patients)

The standard error of the mean is calculated by the standard deviation / square root (number of patients)

$$= 12 / \text{square root } (64) = 12 / 8 = 1.5$$

**Standard error of the mean**

The standard error of the mean (SEM) is a measure of the spread expected for the mean of the observations - i.e. how 'accurate' the calculated sample mean is from the true population mean

Key point

- $SEM = SD / \text{square root } (n)$
- where SD = standard deviation and n = sample size

Therefore the SEM gets smaller as the sample size (n) increases

A confidence interval for the mean can be calculated in a similar way to that for a single observation, i.e. The 95% confidence interval:

- lower limit = mean - (1.96 \* SEM)
- upper limit = mean + (1.96 \* SEM)

Which foramen does the oculomotor nerve go through?

- ☐ A. Superior orbital fissure
- ☐ B. Foramen ovale
- ☐ C. Foramen rotundum
- ☐ D. Optic canal
- ☐ E. Inferior orbital fissure

Next question

### Foramina of the skull

Questions asking about foramina of the skull have come up in the exam in previous years. Below is a brief summary of the major foramina, please see the Wikipedia link for a full list.

Foramen	Bone	Vessels	Nerves
Optic canal	Sphenoid	Ophthalmic artery	Optic nerve (II)
Superior orbital fissure	Sphenoid	Superior ophthalmic vein Inferior ophthalmic vein	Oculomotor nerve (III) Trochlear nerve (IV) lacrimal, frontal and nasociliary branches of ophthalmic nerve (V1) Abducent nerve (VI)
Inferior orbital fissure	Sphenoid and maxilla	Inferior ophthalmic veins Infraorbital artery Infraorbital vein	Zygomatic nerve and infraorbital nerve of maxillary nerve (V2) Orbital branches of pterygopalatine ganglion
Foramen rotundum	Sphenoid	-	Maxillary nerve (V2)
Foramen ovale	Sphenoid	Accessory meningeal artery	Mandibular nerve (V3)
Jugular foramen	Occipital and temporal	Posterior meningeal artery Ascending pharyngeal artery Inferior petrosal sinus Sigmoid sinus Internal jugular vein	Glossopharyngeal nerve (IX) Vagus nerve (X) Accessory nerve (XI)

In terms of the cell cycle, which one of the following phases determine the length of the cell cycle:

<input type="radio"/>	A.	M
<input type="radio"/>	B.	M0
<input type="radio"/>	C.	G1
<input type="radio"/>	D.	S
<input type="radio"/>	E.	G2

Next question

### Cell cycle

M - Mitosis - cell division

G1 - Gap phase 1 - determines length of cell cycle - under influence of p53

S - DNA Synthesis

G2 - Gap phase

A study is performed to assess the correlation between age and systolic blood pressure. Which one of the following statements regarding the calculation of the correlation coefficient,  $r$ , is incorrect?

<input type="radio"/>	A. A value of $r$ greater than 0 implies a positive correlation between age and systolic blood pressure
<input type="radio"/>	B. If $r = 0$ then there is no correlation between systolic blood pressure and age
<input type="radio"/>	C. $r$ may lie anywhere between -1 and 1
<input type="radio"/>	D. May be used to predict systolic blood pressure for a given age
<input type="radio"/>	E. Do not provide evidence of cause and effect

[Next question](#)

Linear regression is needed to predict systolic blood pressure in this scenario

### Correlation and linear regression

Two measurements, or variables, may be plotted on a scatter plot. For example, age may be marked along the x axis and systolic blood pressure along the y axis

#### Correlation

The correlation coefficient (sometimes referred to as Pearson's product-moment coefficient) indicates how closely the points lie to a line drawn through the plotted data. It is denoted by the value  $r$  which may lie anywhere between -1 and 1.

For example

- $r = 1$  - strong positive correlation (e.g. systolic blood pressure always increases with age)
- $r = 0$  - no correlation (e.g. there is no correlation between systolic blood pressure and age)
- $r = -1$  - strong negative correlation (e.g. systolic blood pressure always decreases with age)

Whilst correlation coefficients give information about how one variable may increase or decrease as another variable increases they do not give information about how much the variable will change. They also do not provide information on cause and effect

#### Linear regression

In contrast to the correlation coefficient, linear regression may be used to predict how much one variable changes when a second variable is changed. A regression equation may be formed,  $y = a + bx$ , where

- $y$  = the variable being calculated
- $a$  = the intercept value, when  $x = 0$

- $b$  = the slope of the line or regression coefficient. Simply put, how much  $y$  changes for a given change in  $x$
- $x$  = the second variable

**Question 401 of 402**

Next

A case-control study is being designed to look at the relationship between epilepsy and a new vaccine for varicella. What is the usual outcome measure in a case-control study?

- ☐ A. Numbers needed to harm
- ☐ B. Odds ratio
- ☐ C. Experimental event rate
- ☐ D. Absolute risk increase
- ☐ E. Relative risk

Next question

Case-control studies - odds ratio

**Study design**

The following table highlights the main features of the main types of study:

<b>Randomised controlled trial</b>	Participants randomly allocated to intervention or control group (e.g. standard treatment or placebo)  Practical or ethical problems may limit use
<b>Cohort study</b>	Observational and prospective. Two (or more) are selected according to their exposure to a particular agent (e.g. medicine, toxin) and followed up to see how many develop a disease or other outcome.  The usual outcome measure is the relative risk.  Examples include Framingham Heart Study
<b>Case-control study</b>	Observational and retrospective. Patients with a particular condition (cases) are identified and matched with controls. Data is then collected on past exposure to a possible causal agent for the condition.  The usual outcome measure is the odds ratio.  Inexpensive, produce quick results Useful for studying rare conditions Prone to confounding
<b>Cross-sectional survey</b>	Provide a 'snapshot', sometimes called prevalence studies  Provide weak evidence of cause and effect



### Question 402 of 402

A clinical trial is conducted to study the benefits of a new oral medication to improve the symptoms of patients with chronic obstructive pulmonary disease (COPD). In the trial 300 patients with COPD are given the new medication and a further 300 COPD patients are given a placebo. Three months later they are asked to rate their symptoms using the following scale: *much improved*, *slight improvement*, *no change*, *slight worsening*, *significantly worse*. What is the most appropriate statistical test to see whether the new medication is beneficial?

<input type="radio"/>	A. Mann-Whitney U test
<input type="radio"/>	B. Student's t-test (paired)
<input type="radio"/>	C. Student's t-test (unpaired)
<input type="radio"/>	D. Chi-squared test
<input type="radio"/>	E. Wilcoxon signed-rank test

The first point to note is that the outcome measure is not normally distributed, i.e. it is non-parametric. This excludes the Student's t-tests. We are not comparing percentages/proportions so the chi-squared test is excluded.

The Wilcoxon signed-rank test is used to compares two sets of observations on a single sample or matched samples.

### Significance tests: types

The type of significance test used depends on whether the data is parametric (something which can be measured, usually normally distributed) or non-parametric

#### Parametric tests

- Student's t-test - paired or unpaired
- Pearson's product-moment coefficient - correlation

#### Non-parametric tests

- Mann-Whitney U test - unpaired data
- Wilcoxon signed-rank test - compares two sets of observations on a single sample
- chi-squared test - used to compare proportions or percentages
- Spearman, Kendall rank - correlation

Paired data refers to data obtained from a single group of patients, e.g. Measurement before and after an intervention. Unpaired data comes from two different groups of patients, e.g. Comparing response to different interventions in two groups

### Question 1 of 129

Next

A 41-year-old man develops itchy, polygonal, violaceous papules on the flexor aspect of his forearms. Some of these papules have coalesced to form plaques. What is the most likely diagnosis?

<input type="radio"/>	A. Lichen planus
<input type="radio"/>	B. Scabies
<input type="radio"/>	C. Lichen sclerosus
<input type="radio"/>	D. Morphea
<input type="radio"/>	E. Psoriasis

Next question

#### Lichen

- **planus**: **p**urple, **p**ruritic, **p**apular, **p**olygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- **sclerosus**: itchy white spots typically seen on the vulva of elderly women

#### Lichen planus

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

#### Features

- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon may be seen (new skin lesions appearing at the site of trauma)
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:

- gold
- quinine
- thiazides

#### Management

- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

**Question 2 of 129**[Next](#)

A 30-year-old female in her third trimester of pregnancy mentions during an antenatal appointment that she has noticed an itchy rash around her umbilicus. This is her second pregnancy and she had no similar problems in her first pregnancy. Examination reveals blistering lesions in the peri-umbilical region and on her arms. What is the likely diagnosis?

- |                       |                                      |
|-----------------------|--------------------------------------|
| <input type="radio"/> | A. Seborrhoeic dermatitis            |
| <input type="radio"/> | B. Pompholyx                         |
| <input type="radio"/> | C. Polymorphic eruption of pregnancy |
| <input type="radio"/> | D. Lichen planus                     |
| <input type="radio"/> | E. Pemphigoid gestationis            |

[Next question](#)

Polymorphic eruption of pregnancy is not associated with blistering

Pemphigoid gestationis is the correct answer. Polymorphic eruption of pregnancy is not associated with blistering

**Skin disorders associated with pregnancy****Polymorphic eruption of pregnancy**

- pruritic condition associated with last trimester
- lesions often first appear in abdominal striae
- management depends on severity: emollients, mild potency topical steroids and oral steroids may be used

**Pemphigoid gestationis**

- pruritic blistering lesions
- often develop in peri-umbilical region, later spreading to the trunk, back, buttocks and arms
- usually presents 2nd or 3rd trimester and is rarely seen in the first pregnancy
- oral corticosteroids are usually required

A 62-year-old female is referred to dermatology due to a lesion over her shin. It initially started as a small red papule which later became a deep, red, necrotic ulcer with a violaceous border. What is the likely diagnosis?

<input type="radio"/>	A. Necrobiosis lipoidica diabetorum
<input type="radio"/>	B. Syphilis
<input type="radio"/>	C. Erythema nodosum
<input type="radio"/>	D. Pretibial myxoedema
<input type="radio"/>	E. Pyoderma gangrenosum

[Next question](#)

This is a classic description of pyoderma gangrenosum

### Shin lesions

The differential diagnosis of shin lesions includes the following conditions:

- erythema nodosum
- pretibial myxoedema
- pyoderma gangrenosum
- necrobiosis lipoidica diabetorum

Below are the characteristic features:

#### Erythema nodosum

- symmetrical, erythematous, tender, nodules which heal without scarring
- most common causes are streptococcal infections, sarcoidosis, inflammatory bowel disease and drugs (penicillins, sulphonamides, oral contraceptive pill)

#### Pretibial myxoedema

- symmetrical, erythematous lesions seen in Graves' disease
- shiny, orange peel skin

#### Pyoderma gangrenosum

- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- idiopathic in 50%, may also be seen in inflammatory bowel disease, connective tissue disorders and myeloproliferative disorders

## Necrobiosis lipoidica diabeticorum

- shiny, painless areas of yellow/red skin typically on the shin of diabetics
- often associated with telangiectasia

**Question 4 of 129**

Next

A 39-year-old female has a pigmented mole removed from her leg which histology shows to be a malignant melanoma. What is the single most important prognostic marker?

- ☐ A. Number of episodes of sunburn before the age of 18 years
- ☐ B. Age of patient
- ☐ C. Diameter of melanoma
- ☐ D. Depth of melanoma
- ☐ E. Mutation in the MC1R gene

Next question

Melanoma: the invasion depth of the tumour is the single most important prognostic factor

**Malignant melanoma: prognostic factors**

The invasion depth of a tumour (Breslow depth) is the single most important factor in determining prognosis of patients with malignant melanoma

Breslow Thickness	Approximate 5 year survival
< 1 mm	95-100%
1 - 2 mm	80-96%
2.1 - 4 mm	60-75%
> 4 mm	50%

**Question 5 of 129**

Next

A 62-year-old female is referred due to a long-standing ulcer above the right medial malleolus. Ankle-brachial pressure index readings are as follows:

Right	0.95
Left	0.95

To date it has been managed by the District Nurse with standard dressings. What is the most appropriate management to maximize the likelihood of the ulcer healing?

- ☐ A. Compression bandaging
- ☐ B. Intermittent pneumatic compression
- ☐ C. Hydrocolloid dressings
- ☐ D. Refer to vascular surgeon
- ☐ E. Topical flucloxacillin

Next question

Management of venous ulceration - compression bandaging

The ankle-brachial pressure index readings indicate a reasonable arterial supply and suggest the ulcers are venous in nature.

**Venous ulceration**

Venous ulceration is typically seen above the medial malleolus

**Investigations**

- ankle-brachial pressure index (ABPI) is important in non-healing ulcers to assess for poor arterial flow which could impair healing
- a 'normal' ABPI may be regarded as between 0.9 - 1.2. Values below 0.9 indicate arterial disease. Interestingly, values above 1.3 may also indicate arterial disease, in the form of false-negative results secondary to arterial calcification (e.g. In diabetics)

**Management**

- compression bandaging, usually four layer (only treatment shown to be of real benefit)
- oral pentoxifylline, a peripheral vasodilator, improves healing rate
- small evidence base supporting use of flavinoids
- little evidence to suggest benefit from hydrocolloid dressings, topical growth factors, ultrasound therapy and intermittent pneumatic compression

A 40-year-old man complains of widespread pruritus for the past two weeks. The itching is particularly bad at night. He has no history of note and works in the local car factory. On examination he has noted to have a number of linear erythematous lesions in between his fingers. What is the most likely diagnosis?

<input type="radio"/>	A. Polyurethane dermatitis
<input type="radio"/>	B. Fibreglass exposure
<input type="radio"/>	C. Cimex lectularius infestation (Bed-bugs)
<input type="radio"/>	D. Scabies
<input type="radio"/>	E. Langerhans cell histiocytosis

[Next question](#)

## Scabies

Scabies is caused by the mite *Sarcoptes scabiei* and is spread by prolonged skin contact. It typically affects children and young adults.

The scabies mite burrows into the skin, laying its eggs in the stratum corneum. The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

### Features

- widespread pruritus
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

### Management

- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication

### Patient guidance on treatment (from Clinical Knowledge Summaries)

- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic
- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.



The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation. Patients should be given the following instructions:

- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8-12 hours for permethrin, or for 24 hours for malathion, before washing off
- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

**Question 7 of 129**

Next

A 22-year-old woman presents due to hypopigmented skin lesions on her chest and back. She has recently returned from the south of France and has tanned skin. On examination the lesions are slightly scaly. What is the most likely diagnosis?

<input type="radio"/>	A. Tinea corporis
<input type="radio"/>	B. Pityriasis versicolor
<input type="radio"/>	C. Porphyria cutanea tarda
<input type="radio"/>	D. Lyme disease
<input type="radio"/>	E. Psoriasis

Next question

**Pityriasis versicolor**

Pityriasis versicolor, also called tinea versicolor, is a superficial cutaneous fungal infection caused by *Malassezia furfur* (formerly termed *Pityrosporum ovale*)

**Features**

- most commonly affects trunk
- patches may be hypopigmented, pink or brown (hence versicolor)
- scale is common
- mild pruritus

**Predisposing factors**

- occurs in healthy individuals
- immunosuppression
- malnutrition
- Cushing's

**Management**

- topical antifungal e.g. terbinafine or selenium sulphide
- if extensive disease or failure to respond to topical treatment then consider oral itraconazole

A 67-year-old man with a history of Parkinson's disease presents due to the development of an itchy, red rash on his neck, behind his ears and around the nasolabial folds. He had a similar flare up last winter but did not seek medical attention. What is the most likely diagnosis?

<input type="radio"/>	A. Levodopa associated dermatitis
<input type="radio"/>	B. Seborrhoeic dermatitis
<input type="radio"/>	C. Flexural psoriasis
<input type="radio"/>	D. Acne rosacea
<input type="radio"/>	E. Fixed drug reaction to ropinirole

[Next question](#)

Seborrhoeic dermatitis is more common in patients with Parkinson's disease

### Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called *Malassezia furfur* (formerly known as *Pityrosporum ovale*). It is common, affecting around 2% of the general population

#### Features

- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

#### Associated conditions include

- HIV
- Parkinson's disease

#### Scalp disease management

- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

#### Face and body management

- topical antifungals: e.g. Ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

A 43-year-old man comes for review. A few months ago he developed redness around his nose and cheeks. This is worse after drinking alcohol. He is concerned as one of his work colleagues asked him if he had a drink problem despite him drinking 14 units per week. On examination he has erythema as described above with some pustules on the nose and telangiectasia on the cheeks. What is the most likely diagnosis?

- |                                  |                                 |
|----------------------------------|---------------------------------|
| <input type="radio"/>            | A. Mitral stenosis              |
| <input type="radio"/>            | B. Seborrhoeic dermatitis       |
| <input type="radio"/>            | C. Alcohol-related skin changes |
| <input checked="" type="radio"/> | D. Acne rosacea                 |
| <input type="radio"/>            | E. Systemic lupus erythematosus |

[Next question](#)

This is a typical history of acne rosacea

### Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

#### Features

- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

#### Management

- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

**Question 10 of 129**

Next

A 19-year-old student presents with a three day history of a 1 cm golden, crusted lesion on the border of her lower lip. What is the most suitable management?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Oral co-amoxiclav                |
| <input type="radio"/> | B. Oral penicillin                  |
| <input type="radio"/> | C. Oral flucloxacillin              |
| <input type="radio"/> | D. Oral flucloxacillin + penicillin |
| <input type="radio"/> | E. Topical fusidic acid             |

Next question

Impetigo - topical fusidic acid --> oral flucloxacillin / topical retapamulin

This history is typical of impetigo. As the lesion is small and localised topical fusidic acid is recommended

**Impetigo: management**

Limited, localised disease

- topical fusidic acid is first-line
- topical retapamulin is used second-line if fusidic acid has been ineffective or is not tolerated
- MRSA is not susceptible to either fusidic acid or retapamulin. Topical mupirocin (Bactroban) should therefore be used in this situation

Extensive disease

- oral flucloxacillin
- oral erythromycin if penicillin allergic

A 74-year-old lady with a history of hypothyroidism presents in January with a rash down the right side of her body. On examination an erythematous rash with patches of hyperpigmentation and telangiectasia is found. What is the likely diagnosis?

<input type="radio"/>	A. Erythema marginatum
<input type="radio"/>	B. Herpes zoster
<input type="radio"/>	C. Pretibial myxoedema
<input checked="" type="radio"/>	D. Erythema ab igne
<input type="radio"/>	E. Xanthomata

[Next question](#)

This is a classic presentation of erythema ab igne. Despite the name, pretibial myxoedema is associated with hyperthyroidism rather than hypothyroidism.

Hypothyroidism can make patients feel cold and hence more likely to sit next a heater / fire.

### Erythema ab igne

Erythema ab igne is a skin disorder caused by over exposure to infrared radiation. Characteristic features include reticulated, erythematous patches with hyperpigmentation and telangiectasia. A typical history would be an elderly women who always sits next to an open fire

If the cause is not treated then patients may go on to develop squamous cell skin cancer

A 28-year-old man presents with multiple protuberant lesions around the anus which have been present for about 6 weeks. He reports it is painful when he passes a stool although there is no change in bowel habit. What is the most likely diagnosis?

<input type="radio"/>	A. Haemorrhoids
<input type="radio"/>	B. Anal cancer
<input type="radio"/>	C. Genital warts
<input type="radio"/>	D. Anal skin tags
<input type="radio"/>	E. Crohn's disease

[Next question](#)

Ambiguous questions such as this are common in the MRCP. Whilst a case could be made for any of the answers the most likely cause from the above list, in a 28-year-old male, is genital warts

### Genital warts

Genital warts (also known as condylomata accuminata) are a common cause of attendance at genitourinary clinics. They are caused by the many varieties of the human papilloma virus HPV, especially types 6 & 11. It is now well established that HPV (primarily types 16, 18 & 33) predisposes to cervical cancer.

#### Features

- small (2 - 5 mm) fleshy protuberances which are slightly pigmented
- may bleed or itch

#### Management

- topical podophyllum or cryotherapy are commonly used as first-line treatments depending on the location and type of lesion. Multiple, non-keratinised warts are generally best treated with topical agents whereas solitary, keratinised warts respond better to cryotherapy
- imiquimod is a topical cream which is generally used second line
- genital warts are often resistant to treatment and recurrence is common although the majority of anogenital infections with HPV clear without intervention within 1-2 years

A 25-year-old man presents with a widespread rash over his body. The torso and limbs are covered with multiple erythematous lesions less than 1 cm in diameter which in parts are covered by a fine scale. You note that two weeks earlier he was seen with a sore throat when it was noted that he had exudative tonsillitis. Other than a history of asthma he is normally fit and well. What is the most likely diagnosis?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Pityriasis Rosea      |
| <input type="radio"/> | B. Pityriasis versicolor |
| <input type="radio"/> | C. Syphilis              |
| <input type="radio"/> | D. Discoid eczema        |
| <input type="radio"/> | E. Guttate psoriasis     |

[Next question](#)

### Psoriasis: guttate

Guttate psoriasis is more common in children and adolescents. It may be precipitated by a streptococcal infection 2-4 weeks prior to the lesions appearing

#### Features

- tear drop papules on the trunk and limbs

#### Management

- most cases resolve spontaneously within 2-3 months
- there is no firm evidence to support the use of antibiotics to eradicate streptococcal infection
- topical agents as per psoriasis
- UVB phototherapy
- tonsillectomy may be necessary with recurrent episodes



A 25-year-old man presents with a pruritic skin rash. This has been present for the past few weeks and has responded poorly to an emollient cream. The pruritus is described as 'intense' and has resulted in him having trouble sleeping. On inspecting the skin you notice a combination of papules and vesicles on his buttocks and the extensor aspect of the knees and elbows. What is the most likely diagnosis?

<input type="radio"/>	A. Lichen planus
<input type="radio"/>	B. Chronic plaque psoriasis
<input type="radio"/>	C. Henoch-Schonlein purpura
<input checked="" type="radio"/>	D. Dermatitis herpetiformis
<input type="radio"/>	E. Scabies

[Next question](#)

### Dermatitis herpetiformis

Dermatitis herpetiformis is an autoimmune blistering skin disorder associated with coeliac disease. It is caused by deposition of IgA in the dermis.

#### Features

- itchy, vesicular skin lesions on the extensor surfaces (e.g. elbows, knees buttocks)

#### Diagnosis

- skin biopsy: direct immunofluorescence shows deposition of IgA in a granular pattern in the upper dermis

#### Management

- gluten-free diet
- dapsone

**Question 15 of 129**

Next

A 54-year-old man is referred to the dermatology outpatient department due to a facial rash which has persisted for the past 12 months. On examination there is a symmetrical rash consisting of extensive pustules and papules which affects his nose, cheeks and forehead. What is the most appropriate treatment?

<input type="radio"/>	A. Ciprofloxacin
<input type="radio"/>	B. Isotretinoin
<input type="radio"/>	C. Oxytetracycline
<input type="radio"/>	D. Hydroxychloroquine
<input type="radio"/>	E. Prednisolone

Next question

Acne rosacea treatment:

- mild/moderate: topical metronidazole
- severe/resistant: oral tetracycline

As there is extensive involvement oral oxytetracycline should probably be used rather than topical metronidazole

**Acne rosacea**

Acne rosacea is a chronic skin disease of unknown aetiology

**Features**

- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

**Management**

- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

**Question 16 of 129**

Next

A 23-year-old man presents with a three day history of general malaise and low-grade temperature. Yesterday he developed extensive painful ulceration of his mouth and gums. On examination his temperature is 37.4°C, pulse 84 / min and there is submandibular lymphadenopathy. What is the most likely diagnosis?

<input type="radio"/>	A. Epstein Barr virus
<input type="radio"/>	B. Lichen planus
<input type="radio"/>	C. HIV seroconversion illness
<input type="radio"/>	D. Herpes simplex virus infection
<input type="radio"/>	E. Oral <i>Candida</i>

Next question

This man has gingivostomatitis, a characteristic feature of primary herpes simplex virus infection

**Herpes simplex virus**

There are two strains of the herpes simplex virus (HSV) in humans: HSV-1 and HSV-2. Whilst it was previously thought HSV-1 accounted for oral lesions (cold sores) and HSV-2 for genital herpes it is now known there is considerable overlap

**Features**

- primary infection: may present with a severe gingivostomatitis
- cold sores
- painful genital ulceration

**Management**

- gingivostomatitis: oral aciclovir, chlorhexidine mouthwash
- cold sores: topical aciclovir although the evidence base for this is modest
- genital herpes: oral aciclovir. Some patients with frequent exacerbations may benefit from longer term aciclovir

Which one of the following conditions is most strongly associated with erythema multiforme?

<input type="radio"/>	A. Crohn's disease
<input type="radio"/>	B. Tuberculosis
<input type="radio"/>	C. Sarcoidosis
<input type="radio"/>	D. Herpes simplex virus
<input type="radio"/>	E. Streptococcal infections

Next question

This is difficult as both herpes simplex and streptococcal infections are known causes of erythema multiforme (EM). However, studies suggest that HSV is the trigger in over 50% of cases. Streptococcal infections and sarcoidosis are more strongly associated with erythema nodosum

### Erythema multiforme

#### Features

- target lesions
- initially seen on the back of the hands / feet before spreading to the torso
- upper limbs are more commonly affected than the lower limbs
- pruritus is occasionally seen and is usually mild

If symptoms are severe and involve blistering and mucosal involvement the term Stevens-Johnson syndrome is used.

#### Causes

- viruses: herpes simplex virus (the most common cause), Orf\*
- idiopathic
- bacteria: Mycoplasma, *Streptococcus*
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill, nevirapine
- connective tissue disease e.g. Systemic lupus erythematosus
- sarcoidosis
- malignancy

\*Orf is a skin disease of sheep and goats caused by a parapox virus

Which of the following conditions is most associated with onycholysis?

<input type="radio"/>	A. Bullous pemphigoid
<input type="radio"/>	B. Raynaud's disease
<input type="radio"/>	C. Osteogenesis imperfecta
<input type="radio"/>	D. Oesophageal cancer
<input type="radio"/>	E. Scabies

Next question

Raynaud's disease causes onycholysis, as can any cause of impaired circulation

### Onycholysis

Onycholysis describes the separation of the nail plate from the nail bed

#### Causes

- idiopathic
- trauma e.g. Excessive manicuring
- infection: especially fungal
- skin disease: psoriasis, dermatitis
- impaired peripheral circulation e.g. Raynaud's
- systemic disease: hyper- and hypothyroidism

**Question 19 of 129**

Next

A 34-year-old man presents for the removal of a mole. Where on the body are keloid scars most likely to form?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Sternum                  |
| <input type="radio"/> | B. Lower back               |
| <input type="radio"/> | C. Abdomen                  |
| <input type="radio"/> | D. Flexor surfaces of limbs |
| <input type="radio"/> | E. Scalp                    |

Next question

Keloid scars are most common on the sternum

**Keloid scars**

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

**Predisposing factors**

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk

Keloid scars are less likely if incisions are made along relaxed skin tension lines\*

**Treatment**

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

\*Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

A 45-year-old woman presents for review. She has noticed a number of patches of 'pale skin' on her hands over the past few weeks. The patient has tried using an emollient and topical hydrocortisone with no result. On examination you note a number of hypopigmented patches on the dorsum of both hands. Her past medical history includes thyrotoxicosis for which she takes carbimazole and thyroxine. What is the most likely causes of her symptoms?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Vitiligo                             |
| <input type="radio"/> | B. Carbimazole-induced hypopigmentation |
| <input type="radio"/> | C. Leukopaenia-induced fungal infection |
| <input type="radio"/> | D. Idiopathic guttate hypomelanosis     |
| <input type="radio"/> | E. Addison disease                      |

[Next question](#)

Vitiligo is more common in patients with known autoimmune conditions such as thyrotoxicosis. There is nothing else in the history to suggest Addison disease.

### Vitiligo

Vitiligo is an autoimmune condition which results in the loss of melanocytes and consequent depigmentation of the skin. It is thought to affect around 1% of the population and symptoms typically develop by the age of 20-30 years.

#### Features

- well demarcated patches of depigmented skin
- the peripheries tend to be most affected
- trauma may precipitate new lesions (Koebner phenomenon)

#### Associated conditions

- type 1 diabetes mellitus
- Addison's disease
- autoimmune thyroid disorders
- pernicious anaemia
- alopecia areata

#### Management

- sun block for affected areas of skin
- camouflage make-up
- topical corticosteroids may reverse the changes if applied early
- there may also be a role for topical tacrolimus and phototherapy, although caution needs to be exercised with light-skinned patients

Which one of the following complications is most associated with psoralen + ultraviolet A light (PUVA) therapy?

- |                       |                         |
|-----------------------|-------------------------|
| <input type="radio"/> | A. Squamous cell cancer |
| <input type="radio"/> | B. Osteoporosis         |
| <input type="radio"/> | C. Basal cell cancer    |
| <input type="radio"/> | D. Dermoid cysts        |
| <input type="radio"/> | E. Malignant melanoma   |

Next question

The most significant complication of PUVA therapy for psoriasis is squamous cell skin cancer.

### Psoriasis: management

SIGN released guidelines in 2010 on the management of psoriasis and psoriatic arthropathy. Please see the link for more details.

#### Chronic plaque psoriasis

- regular emollients may help to reduce scale loss and reduce pruritus
- for acute control SIGN recommend: 'Short term intermittent use of a potent topical corticosteroid or a combined potent corticosteroid plus calcipotriol

ointment is recommended to gain rapid improvement in plaque psoriasis.'

- 'For long term topical treatment of plaque psoriasis a vitamin D analogue (e.g. Calcipotriol) is recommended.'
- 'If a vitamin D analogue is ineffective or not tolerated then consider coal tar (solution, cream or lotion), tazarotene gel, or short contact dithranol (30 minute exposure in patients with a small number of relatively large plaques of psoriasis).

#### Steroids in psoriasis

- topical steroids are commonly used in flexural psoriasis and there is also a role for mild steroids in facial psoriasis. If steroids are ineffective for these conditions vitamin D analogues or tacrolimus ointment should be used second line
- SIGN caution against the long term use of potent or very potent topical steroids due to the risk of side-effects

#### Scalp psoriasis



- for short term control SIGN recommend either the use of potent topical corticosteroids or a combination of a potent corticosteroid and a vitamin D

analogue

- 'For patients with thick scaling of the scalp, initial treatment with overnight application of salicylic acid, tar preparations, or oil preparations (eg olive oil, coconut oil) to remove thick scale is recommended.

## **Secondary care management**

Phototherapy

- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy

- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab
- ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials

Mechanism of action of commonly used drugs:

- coal tar: probably inhibit DNA synthesis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

A 38-year-old woman with a history of rheumatoid arthritis and epilepsy presents with generalised increased hair growth over her trunk and arms. Which one of the following drugs is associated with hypertrichosis?

<input type="radio"/>	A. Sodium valproate
<input type="radio"/>	B. Prednisolone
<input type="radio"/>	C. Phenytoin
<input type="radio"/>	D. Ciclosporin
<input type="radio"/>	E. Methotrexate

[Next question](#)

Phenytoin is associated with hirsutism rather than hypertrichosis

### Hirsutism and hypertrichosis

/hirsutism is often used to describe androgen-dependent hair growth in women, with hypertrichosis being used for androgen-independent hair growth

Polycystic ovarian syndrome is the most common causes of hirsutism. Other causes include:

- Cushing's syndrome
- congenital adrenal hyperplasia
- androgen therapy
- obesity: due to peripheral conversion oestrogens to androgens
- adrenal tumour
- androgen secreting ovarian tumour
- drugs: phenytoin

### Assessment of hirsutism

- Ferriman-Gallwey scoring system: 9 body areas are assigned a score of 0 - 4, a score > 15 is considered to indicate moderate or severe hirsutism

### Management of hirsutism

- advise weight loss if overweight
- cosmetic techniques such as waxing/bleaching - not available on the NHS
- consider using combined oral contraceptive pills such as co-cyprindiol (Dianette) or ethinylestradiol and drospirenone (Yasmin). Co-cyprindiol should not be used long-term due to the increased risk of venous thromboembolism
- facial hirsutism: topical eflornithine - contraindicated in pregnancy and breast-feeding

## Causes of hypertrichosis

- drugs: minoxidil, ciclosporin, diazoxide
- congenital hypertrichosis lanuginosa, congenital hypertrichosis terminalis
- porphyria cutanea tarda
- anorexia nervosa

**Question 23 of 129**

Next

A 64-year-old patient is referred to dermatology outpatients due to a rash. A diagnosis necrolytic migratory erythema is made. What is the most likely underlying diagnosis?

- ☐ A. Gastrinoma
- ☐ B. Lung cancer
- ☐ C. Glucagonoma
- ☐ D. Pancreatic cancer
- ☐ E. Lymphoma

Next question

**Skin disorders associated with malignancy**

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	Associated malignancies
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Ovarian and lung cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

A 31-year-old woman develops with painful, purple lesions on her shins. Which one of the following medications is most likely to be responsible?

<input type="radio"/>	A. Montelukast
<input type="radio"/>	B. Lansoprazole
<input type="radio"/>	C. Combined oral contraceptive pill
<input type="radio"/>	D. Sodium valproate
<input type="radio"/>	E. Carbimazole

[Next question](#)

## Erythema nodosum

### Overview

- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

### Causes

- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

Which one of the following conditions is least likely to be associated with pyoderma gangrenosum?

<input type="radio"/>	A. Ulcerative colitis
<input type="radio"/>	B. Syphilis
<input type="radio"/>	C. Lymphoma
<input type="radio"/>	D. IgA monoclonal gammopathy
<input type="radio"/>	E. Rheumatoid arthritis

Next question

Syphilis is not commonly associated with pyoderma gangrenosum

### Pyoderma gangrenosum

#### Features

- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

#### Causes\*

- idiopathic in 50%
- inflammatory bowel disease: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

#### Management

- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

\*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

**Question 26 of 129**

Next

A 36-year-old woman is reviewed. She presented 4 weeks ago with itchy dry skin on her arms and was diagnosed as having atopic eczema. She was prescribed hydrocortisone 1% cream with an emollient. Unfortunately there has been no improvement in her symptoms. What is the next step in management, alongside continued regular use of an emollient?

- ☐ A. Betamethasone valerate 0.1%
- ☐ B. Clobetasone butyrate 0.05%
- ☐ C. Clobetasol propionate 0.05%
- ☐ D. Topical tetracycline
- ☐ E. Regular wet wraps

Next question

**Topical steroids**

- moderate: Clobetasone butyrate 0.05%
- potent: Betamethasone valerate 0.1%
- very potent: Clobetasol propionate 0.05%

Clobetasone butyrate 0.05% is a moderately potent topical steroid and would be the most suitable next step in management. It is important to note the potency difference between two very similar sounding steroids - Clobetasone butyrate 0.05% (moderate) and Clobetasol propionate 0.05% (very potent)

**Eczema: topical steroids**

Use weakest steroid cream which controls patients symptoms

The table below shows topical steroids by potency

Mild	Moderate	Potent	Very potent
Hydrocortisone 0.5-2.5%	Betamethasone valerate 0.025% (Betnovate RD)  Clobetasone butyrate 0.05% (Eumovate)	Fluticasone propionate 0.05% (Cutivate)  Betamethasone valerate 0.1% (Betnovate)	Clobetasol propionate 0.05% (Dermovate)

**Finger tip rule**

- 1 finger tip unit (FTU) = 0.5 g, sufficient to treat a skin area about twice that of the flat of an adult hand

## Topical steroid doses for eczema in adults

Area of skin	Fingertip units per dose
Hand and fingers (front and back)	1.0
A foot (all over)	2.0
Front of chest and abdomen	7.0
Back and buttocks	7.0
Face and neck	2.5
An entire arm and hand	4.0
An entire leg and foot	8.0

The BNF makes recommendation on the quantity of topical steroids that should be prescribed for an adult for a single daily application for 2 weeks:

Area	Amount
Face and neck	15 to 30 g
Both hands	15 to 30 g
Scalp	15 to 30 g
Both arms	30 to 60 g
Both legs	100 g
Trunk	100 g
Groin and genitalia	15 to 30 g



A 54-year-old man presents with a brown velvety rash on the back of his neck around his axilla. A clinical diagnosis of acanthosis nigricans is made. Which one of the following conditions is most associated with this kind of rash?

<input type="radio"/>	A. Hypothyroidism
<input type="radio"/>	B. Psoriasis
<input type="radio"/>	C. Tuberculosis
<input type="radio"/>	D. Ulcerative colitis
<input type="radio"/>	E. Acute pancreatitis

[Next question](#)

### Acanthosis nigricans

Describes symmetrical, brown, velvety plaques that are often found on the neck, axilla and groin

#### Causes

- gastrointestinal cancer
- insulin-resistant diabetes mellitus
- obesity
- polycystic ovarian syndrome
- acromegaly
- Cushing's disease
- hypothyroidism
- familial
- Prader-Willi syndrome
- drugs: oral contraceptive pill, nicotinic acid

A 67-year-old man who is a retired builder presents following the development of a number of red, scaly lesions on his left temple. These were initially small and flat but are now erythematous and rough to touch. What is the most likely diagnosis?

<input type="radio"/>	A. Pityriasis versicolor
<input type="radio"/>	B. Seborrhoeic keratosis
<input type="radio"/>	C. Polymorphous light eruption
<input checked="" type="radio"/>	D. Actinic keratoses
<input type="radio"/>	E. Malignant melanoma

[Next question](#)

### Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

#### Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

#### Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

### Question 29 of 129

Next

A 85-year-old lady presents to dermatology clinic complaining of itchy white plaques affecting her vulva. There is no history of vaginal discharge or bleeding. A similar plaque is also seen on her inner thigh. What is the likely diagnosis?

<input type="radio"/>	A. <i>Candida</i>
<input type="radio"/>	B. Lichen planus
<input type="radio"/>	C. Lichen sclerosus
<input type="radio"/>	D. Herpes simplex
<input type="radio"/>	E. Seborrhoeic dermatitis

Next question

#### Lichen

- **planus**: **p**urple, **p**ruritic, **p**apular, **p**olygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- **sclerosus**: itchy white spots typically seen on the vulva of elderly women

The correct answer is lichen sclerosus. *Candida* may cause pruritus and white plaques but lesions would not also be seen on her inner thigh

#### Lichen sclerosus

Lichen sclerosus was previously termed lichen sclerosus et atrophicus. It is an inflammatory condition which usually affects the genitalia and is more common in elderly females. Lichen sclerosus leads to atrophy of the epidermis with white plaques forming

#### Features

- itch is prominent

A biopsy is often performed to exclude other diagnoses

#### Management

- topical steroids and emollients
- increased risk of vulval cancer

A 26-year-old newly qualified nurse presents as she has developed a bilateral erythematous rash on both hands. She has recently emigrated from the Philippines and has no past medical history of note. A diagnosis of contact dermatitis is suspected. What is the most suitable to test to identify the underlying cause?

- ☐ A. Radioallergosorbent test (RAST)
- ☐ B. Latex IgM levels
- ☐ C. Skin prick test
- ☐ D. Urinary porphyrins
- ☐ E. Skin patch test

[Next question](#)

The skin patch test is useful in this situation as it may also identify for irritants, not just allergens

### Allergy tests

<b>Skin prick test</b>	<p>Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes</p> <p>Useful for food allergies and also pollen</p>
<b>Radioallergosorbent test (RAST)</b>	<p>Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive)</p> <p>Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom</p> <p>Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines</p>
<b>Skin patch testing</b>	<p>Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The patches are removed 48 hours later with the results being read by a dermatologist after a further 48 hours</p>

A 43-year-old man is admitted to the Emergency Department with a rash and feeling generally unwell. He is known to have epilepsy and his medication was recently changed to phenytoin three weeks ago. Around one week ago he started to develop mouth ulcers associated with malaise and a cough. Two days ago he started to develop a widespread red rash which has now coalesced to form large fluid-filled blisters, covering around 30% of his body area. The lesions separate when slight pressure is applied. On examination his temperature is 38.3°C and pulse 126 / min. Blood results show:

Na <sup>+</sup>	144 mmol/l
K <sup>+</sup>	4.2 mmol/l
Bicarbonate	19 mmol/l
Urea	13.4 mmol/l
Creatinine	121 µmol/l

What is the most likely diagnosis?

- ☐ A. Phenytoin-induced neutropaenia
- ☐ B. Drug-induced lupus
- ☐ C. Kawasaki disease
- ☐ D. Toxic epidermal necrolysis
- ☐ E. Staphylococcal Scalded Skin syndrome

Next question

### Toxic epidermal necrolysis

Toxic epidermal necrolysis (TEN) is a potentially life-threatening skin disorder that is most commonly seen secondary to a drug reaction. In this condition the skin develops a scalded appearance over an extensive area. Some authors consider TEN to be the severe end of a spectrum of skin disorders which includes erythema multiforme and Stevens-Johnson syndrome

#### Features

- systemically unwell e.g. pyrexia, tachycardic
- positive Nikolsky's sign: the epidermis separates with mild lateral pressure

#### Drugs known to induce TEN

- phenytoin
- sulphonamides

- allopurinol
- penicillins
- carbamazepine
- NSAIDs

## Management

- stop precipitating factor
- supportive care, often in intensive care unit
- intravenous immunoglobulin has been shown to be effective and is now commonly used first-line
- other treatment options include: immunosuppressive agents (ciclosporin and cyclophosphamide), plasmapheresis

**Question 32 of 129**[Next](#)

A 34-year-old man presents to dermatology clinic with an itchy rash on his palms. He has also noticed the rash around the site of a recent scar on his forearm. Examination reveals papules with a white-lace pattern on the surface. Some isolated white streaks are also noted on the mucous membranes of the mouth. What is the diagnosis?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Lichen planus    |
| <input type="radio"/> | B. Scabies          |
| <input type="radio"/> | C. Lichen sclerosus |
| <input type="radio"/> | D. Morphea          |
| <input type="radio"/> | E. Pityriasis rosea |

[Next question](#)**Lichen**

- **planus**: purple, pruritic, papular, polygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- **sclerosus**: itchy white spots typically seen on the vulva of elderly women

This is a typical history of lichen planus.

**Lichen planus**

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

**Features**

- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon may be seen (new skin lesions appearing at the site of trauma)
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:

- gold
- quinine
- thiazides

## Management

- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression



An 18-year-old female is reviewed in the dermatology clinic complaining of scalp hair loss. Which one of the following conditions is least likely to be responsible?

<input type="radio"/>	A. Porphyria cutanea tarda
<input type="radio"/>	B. Discoid lupus
<input type="radio"/>	C. Tinea capitis
<input type="radio"/>	D. Alopecia areata
<input type="radio"/>	E. Telogen effluvium

[Next question](#)

Porphyria cutanea tarda is a recognised cause of hypertrichosis

## Alopecia

Alopecia may be divided into scarring (destruction of hair follicle) and non-scarring (preservation of hair follicle)

### Scarring alopecia

- trauma, burns
- radiotherapy
- lichen planus
- discoid lupus
- tinea capitis\*

### Non-scarring alopecia

- male-pattern baldness
- drugs: cytotoxic drugs, carbimazole, heparin, oral contraceptive pill, colchicine
- nutritional: iron and zinc deficiency
- autoimmune: alopecia areata
- telogen effluvium (hair loss following stressful period e.g. surgery)
- trichotillomania

\*scarring would develop in untreated tinea capitis if a kerion develops

A 55-year-old female is referred to dermatology due to a lesions over both shins. On examination symmetrical erythematous lesions are found with an orange peel texture. What is the likely diagnosis?

<input type="radio"/>	A. Pretibial myxoedema
<input type="radio"/>	B. Pyoderma gangrenosum
<input type="radio"/>	C. Necrobiosis lipoidica diabetorum
<input type="radio"/>	D. Erythema nodosum
<input type="radio"/>	E. Syphilis

[Next question](#)

### Shin lesions

The differential diagnosis of shin lesions includes the following conditions:

- erythema nodosum
- pretibial myxoedema
- pyoderma gangrenosum
- necrobiosis lipoidica diabetorum

Below are the characteristic features:

#### Erythema nodosum

- symmetrical, erythematous, tender, nodules which heal without scarring
- most common causes are streptococcal infections, sarcoidosis, inflammatory bowel disease and drugs (penicillins, sulphonamides, oral contraceptive pill)

#### Pretibial myxoedema

- symmetrical, erythematous lesions seen in Graves' disease
- shiny, orange peel skin

#### Pyoderma gangrenosum

- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- idiopathic in 50%, may also be seen in inflammatory bowel disease, connective tissue disorders and myeloproliferative disorders

## Necrobiosis lipoidica diabeticorum

- shiny, painless areas of yellow/red skin typically on the shin of diabetics
- often associated with telangiectasia

Which of the following skin conditions is not associated with diabetes mellitus?

<input type="radio"/>	A. Necrobiosis lipoidica
<input type="radio"/>	B. Sweet's syndrome
<input type="radio"/>	C. Granuloma annulare
<input type="radio"/>	D. Vitiligo
<input type="radio"/>	E. Lipoatrophy

Next question

Sweet's syndrome is also known as acute febrile neutrophilic dermatosis has a strong association with acute myeloid leukaemia. It is not associated with diabetes mellitus

### Skin disorders associated with diabetes

Note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is often not included in a differential of potential causes

Necrobiosis lipoidica

- shiny, painless areas of yellow/red/brown skin typically on the shin
- often associated with surrounding telangiectasia

Infection

- candidiasis
- staphylococcal

Neuropathic ulcers

Vitiligo

Lipoatrophy

Granuloma annulare\*

- papular lesions that are often slightly hyperpigmented and depressed centrally

\*it is not clear from recent studies if there is actually a significant association between diabetes mellitus and granuloma annulare, but it is often listed in major textbooks

Which of the following skin disorders is least associated with tuberculosis?

<input type="radio"/>	A. Scrofuloderma
<input type="radio"/>	B. Erythema nodosum
<input type="radio"/>	C. Lupus vulgaris
<input type="radio"/>	D. Verrucosa cutis
<input type="radio"/>	E. Lupus pernio

Next question

Lupus pernio is sometimes seen in sarcoidosis but is not associated with tuberculosis

#### Skin disorders associated with tuberculosis

Possible skin disorders

- lupus vulgaris (accounts for 50% of cases)
- erythema nodosum
- scarring alopecia
- scrofuloderma: breakdown of skin overlying a tuberculous focus
- verrucosa cutis
- gumma

Lupus vulgaris is the most common form of cutaneous TB seen in the Indian subcontinent. It generally occurs on the face and is common around the nose and mouth. The initial lesion is an erythematous flat plaque which gradually becomes elevated and may ulcerate later

A 62-year-old male is referred to dermatology with a lesion over his shin. On examination shiny, painless areas of yellow skin over the shin are found with abundant telangiectasia. What is the most likely diagnosis?

<input type="radio"/>	A. Pretibial myxoedema
<input checked="" type="radio"/>	B. Necrobiosis lipoidica diabetorum
<input type="radio"/>	C. Erythema nodosum
<input type="radio"/>	D. Pyoderma gangrenosum
<input type="radio"/>	E. Syphilis

[Next question](#)

### Shin lesions

The differential diagnosis of shin lesions includes the following conditions:

- erythema nodosum
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- pyoderma gangrenosum
- necrobiosis lipoidica diabetorum

Below are the characteristic features:

#### Erythema nodosum

- symmetrical, erythematous, tender, nodules which heal without scarring
- most common causes are streptococcal infections, sarcoidosis, inflammatory bowel disease and drugs (penicillins, sulphonamides, oral contraceptive pill)

#### Pretibial myxoedema

- symmetrical, erythematous lesions seen in Graves' disease
- shiny, orange peel skin

#### Pyoderma gangrenosum

- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- idiopathic in 50%, may also be seen in inflammatory bowel disease, connective tissue disorders and myeloproliferative disorders

## Necrobiosis lipoidica diabeticorum

- shiny, painless areas of yellow/red skin typically on the shin of diabetics
- often associated with telangiectasia

Which one of the following conditions is least associated with pruritus?

- ☐ A. Pemphigus vulgaris
- ☐ B. Iron-deficiency anaemia
- ☐ C. Polycythaemia
- ☐ D. Chronic renal failure
- ☐ E. Scabies

Next question

Pemphigus vulgaris is an autoimmune bullous disease of the skin. It is not commonly associated with pruritus

### Pruritus

The table below lists the main characteristics of the most important causes of pruritus

<b>Liver disease</b>	History of alcohol excess Stigmata of chronic liver disease: spider naevi, bruising, palmar erythema, gynaecomastia etc Evidence of decompensation: ascites, jaundice, encephalopathy
<b>Iron deficiency anaemia</b>	Pallor Other signs: koilonychia, atrophic glossitis, post-cricoid webs, angular stomatitis
<b>Polycythaemia</b>	Pruritus particularly after warm bath 'Ruddy complexion' Gout Peptic ulcer disease
<b>Chronic kidney disease</b>	Lethargy & pallor Oedema & weight gain Hypertension
<b>Lymphoma</b>	Night sweats Lymphadenopathy Splenomegaly, hepatomegaly Fatigue

Other causes:

- hyper- and hypothyroidism
- diabetes
- pregnancy
- 'senile' pruritus
- urticaria
- skin disorders: eczema, scabies, psoriasis, pityriasis rosea



A 24-year-old female with a history of anorexia nervosa presents with red crusted lesions around the corner of her mouth and below her lower lip. What is she most likely to be deficient in?

<input type="radio"/>	A. Zinc
<input type="radio"/>	B. Tocopherol
<input type="radio"/>	C. Pantothenic acid
<input type="radio"/>	D. Thiamine
<input type="radio"/>	E. Magnesium

[Next question](#)

Vitamin B2 (riboflavin) deficiency may also cause angular cheilosis.

### Zinc deficiency

#### Features

- perioral dermatitis: red, crusted lesions
- acrodermatitis
- alopecia
- short stature
- hypogonadism
- hepatosplenomegaly
- geophagia (ingesting clay/soil)
- cognitive impairment

Which one of the following statements regarding acne vulgaris is incorrect?

<input type="radio"/>	A. Follicular epidermal hyperproliferation results in obstruction of the pilosebaceous follicle
<input type="radio"/>	B. Acne vulgaris affects at least 80% of teenagers
<input type="radio"/>	C. Propionibacterium acnes is an anaerobic bacterium
<input type="radio"/>	D. Typical lesions include comedones and pustules
<input type="radio"/>	E. Beyond the age of 25 years acne vulgaris is more common in males

Next question

Acne is actually more common in females after the age of 25 years

### Acne vulgaris

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicle with keratin plugs which results in comedones, inflammation and pustules.

#### Epidemiology

- affects around 80-90% of teenagers, 60% of whom seek medical advice
- acne may also persist beyond adolescence, with 10-15% of females and 5% of males over 25 years old being affected

#### Pathophysiology is multifactorial

- follicular epidermal hyperproliferation resulting in the formation of a keratin plug. This in turn causes obstruction of the pilosebaceous follicle. Activity of sebaceous glands may be controlled by androgen, although levels are often normal in patients with acne
- colonisation by the anaerobic bacterium Propionibacterium acnes
- inflammation

A 23-year-old man presents with an itchy skin condition. Which one of the following is not part of the UK Working Party Diagnostic Criteria for atopic eczema?

<input type="radio"/>	A. History of asthma
<input type="radio"/>	B. Responds to topical steroids
<input type="radio"/>	C. History of flexural involvement
<input type="radio"/>	D. Onset below age 2 years
<input type="radio"/>	E. History of generally dry skin

[Next question](#)

Whilst response to topical steroids provides useful clinical information it is not part of the diagnostic criteria. A wide variety of skin conditions can improve with topical steroid therapy.

### Eczema: diagnosis

#### UK Working Party Diagnostic Criteria for Atopic Eczema

An itchy skin condition in the last 12 months

Plus three or more of

- onset below age 2 years\*
- history of flexural involvement\*\*
- history of generally dry skin
- personal history of other atopic disease\*\*\*
- visible flexural dermatitis

\*not used in children under 4 years

\*\*or dermatitis on the cheeks and/or extensor areas in children aged 18 months or under

\*\*\*in children aged under 4 years, history of atopic disease in a first degree relative may be included

A 62-year-old with a history of acne rosacea presents for advice regarding treatment. Which one of the following interventions has the least role in management?

<input type="radio"/>	A. Camouflage creams
<input type="radio"/>	B. Topical metronidazole
<input type="radio"/>	C. Low-dose topical corticosteroids
<input type="radio"/>	D. Laser therapy
<input type="radio"/>	E. Use of high-factor sun block

[Next question](#)

## Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

### Features

- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

### Management

- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia

A 26-year-old man who is HIV positive is noted to have developed seborrhoeic dermatitis. Which of the following two complications are most associated with this condition?

<input type="radio"/>	A. Alopecia and otitis externa
<input type="radio"/>	B. Blepharitis and otitis externa
<input type="radio"/>	C. Photosensitivity and alopecia
<input type="radio"/>	D. Photosensitivity and blepharitis
<input type="radio"/>	E. Blepharitis and alopecia

[Next question](#)

Alopecia is not commonly seen in seborrhoeic dermatitis, but may develop if a severe secondary infection develops

### Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called *Malassezia furfur* (formerly known as *Pityrosporum ovale*). It is common, affecting around 2% of the general population

#### Features

- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

#### Associated conditions include

- HIV
- Parkinson's disease

#### Scalp disease management

- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

#### Face and body management

- topical antifungals: e.g. Ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

A 26-year-old male presents with a rash. Examination reveals erythematous oval lesions on his back and upper arms which have a slight scale just inside the edge. They vary in size from 1 to 5 cm in diameter. What is the most likely diagnosis?

<input type="radio"/>	A. Lichen planus
<input type="radio"/>	B. Guttate psoriasis
<input type="radio"/>	C. Lichen sclerosis
<input type="radio"/>	D. Pityriasis rosea
<input type="radio"/>	E. Pityriasis versicolor

[Next question](#)

The skin lesions seen in pityriasis rosea are generally larger than those found in guttate psoriasis and scaling is typically confined to just inside the edges

### Pityriasis rosea

#### Overview

- cause unknown, herpes hominis virus 7 (HHV-7) a possibility
- tends to affect young adults

#### Features

- herald patch (usually on trunk)
- followed by erythematous, oval, scaly patches which follow a characteristic distribution with the longitudinal diameters of the oval lesions running parallel to the line of Langer. This may produce a 'fir-tree' appearance

#### Management

- self-limiting, usually disappears after 4-6 weeks

Which of the following statements regarding psoriasis is incorrect?

<input type="radio"/>	A. Often occurs on extensor surfaces
<input type="radio"/>	B. Psoriatic arthropathy may occur prior to the development of skin lesions
<input type="radio"/>	C. Mediated by type 2 helper T cells
<input type="radio"/>	D. Abnormal T cell activity stimulates keratinocyte proliferation
<input type="radio"/>	E. Nail signs include pitting and onycholysis

Next question

Psoriasis is mediated by type 1 helper T cells which are involved in the cell mediated response, rather than type 2 helper T cells

## Psoriasis

Psoriasis is a common and chronic skin disorder. It generally presents with red, scaly patches on the skin although it is now recognised that patients with psoriasis are at increased risk of arthritis and cardiovascular disease.

### Pathophysiology

- multifactorial and not yet fully understood
- genetic: associated HLA-B13, -B17, and -Cw6. Strong concordance (70%) in identical twins
- immunological: abnormal T cell activity stimulates keratinocyte proliferation. There is increasing evidence this may be mediated by a novel group of T helper cells producing IL-17, designated Th17. These cells seem to be a third T-effector cell subset in addition to Th1 and Th2
- environmental: it is recognised that psoriasis may be worsened (e.g. Skin trauma, stress), triggered (e.g. Streptococcal infection) or improved (e.g. Sunlight) by environmental factors

### Recognised subtypes of psoriasis

- plaque psoriasis: the most common sub-type resulting in the typical well demarcated red, scaly patches affecting the extensor surfaces, sacrum and scalp
- flexural psoriasis: in contrast to plaque psoriasis the skin is smooth
- guttate psoriasis: transient psoriatic rash frequently triggered by a streptococcal infection. Multiple red, teardrop lesions appear on the body
- pustular psoriasis: commonly occurs on the palms and soles

### Other features

- nail signs: pitting, onycholysis
- arthritis

## Complications

- psoriatic arthropathy (around 10%)
- increased incidence of metabolic syndrome
- increased incidence of cardiovascular disease
- psychological distress



A 24-year-old woman presents due to a rash on her neck and forehead. She returned from a holiday in Cyprus 1 week ago and had her hair dyed 2 days ago. On examination there is a weepy, vesicular rash around her hairline although the scalp itself is not badly affected. What is the most likely diagnosis?

<input type="radio"/>	A. Cutaneous leishmaniasis
<input type="radio"/>	B. Irritant contact dermatitis
<input type="radio"/>	C. Allergic contact dermatitis
<input type="radio"/>	D. Syphilis
<input type="radio"/>	E. Photocontact dermatitis

[Next question](#)

### Contact dermatitis

There are two main types of contact dermatitis

- irritant contact dermatitis: common - non-allergic reaction due to weak acids or alkalis (e.g. detergents). Often seen on the hands. Erythema is typical, crusting and vesicles are rare
- allergic contact dermatitis: type IV hypersensitivity reaction. Uncommon - often seen on the head following hair dyes. Presents as an acute weeping eczema which predominately affects the margins of the hairline rather than the hairy scalp itself. Topical treatment with a potent steroid is indicated

Cement is a frequent cause of contact dermatitis. The alkaline nature of cement may cause an irritant contact dermatitis whilst the dichromates in cement also can cause an allergic contact dermatitis

Which of the following conditions is least likely to exhibit the Koebner phenomenon?

<input type="radio"/>	A. Vitiligo
<input type="radio"/>	B. Molluscum contagiosum
<input type="radio"/>	C. Lichen planus
<input type="radio"/>	D. Psoriasis
<input type="radio"/>	E. Lupus vulgaris

[Next question](#)

Lupus vulgaris is not associated with the Koebner phenomenon

### Koebner phenomenon

The Koebner phenomenon describes skin lesions which appear at the site of injury. It is seen in:

- psoriasis
- vitiligo
- warts
- lichen planus
- lichen sclerosus
- molluscum contagiosum

A 21-year-old woman who is 16 weeks pregnant present with worsening acne which she is finding distressing. She is currently using topical benzyl peroxide with limited effect. On examination there is widespread non-inflammatory lesions and pustules on her face. What is the most appropriate next management step?

<input type="radio"/>	A. Oral trimethoprim
<input type="radio"/>	B. Oral lymecycline
<input type="radio"/>	C. Oral erythromycin
<input type="radio"/>	D. Topical retinoid
<input type="radio"/>	E. Oral doxycycline

[Next question](#)

Oral erythromycin may be used for acne in pregnancy. The other drugs are contraindicated

### Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicles with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. Oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Which one of the following factors would predispose a patient to forming keloid scars?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Having white skin                          |
| <input type="radio"/> | B. Incisions along relaxed skin tension lines |
| <input type="radio"/> | C. Being aged 20-40 years                     |
| <input type="radio"/> | D. Being female                               |
| <input type="radio"/> | E. Having a wound on the lower back           |

Next question

Keloid scars - more common in young, black, male adults

### Keloid scars

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

#### Predisposing factors

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk

Keloid scars are less likely if incisions are made along relaxed skin tension lines\*

#### Treatment

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

\*Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

A 49-year-old man is reviewed in the dermatology clinic complaining of losing hair. Examination reveals generalised scalp hair loss that does not follow the typical male-pattern distribution. Which one of the following medications is least likely to be responsible?

<input type="radio"/>	A. Colchicine
<input type="radio"/>	B. Cyclophosphamide
<input type="radio"/>	C. Heparin
<input type="radio"/>	D. Carbimazole
<input type="radio"/>	E. Phenytoin

[Next question](#)

Phenytoin is a recognised cause of hirsutism, rather than alopecia

## Alopecia

Alopecia may be divided into scarring (destruction of hair follicle) and non-scarring (preservation of hair follicle)

### Scarring alopecia

- trauma, burns
- radiotherapy
- lichen planus
- discoid lupus
- tinea capitis\*

### Non-scarring alopecia

- male-pattern baldness
- drugs: cytotoxic drugs, carbimazole, heparin, oral contraceptive pill, colchicine
- nutritional: iron and zinc deficiency
- autoimmune: alopecia areata
- telogen effluvium (hair loss following stressful period e.g. surgery)
- trichotillomania

\*scarring would develop in untreated tinea capitis if a kerion develops

A 34-year-old man presents with a three week history of an intensely itchy rash on the back of his elbows. On examination he has a symmetrical vesicular rash on the extensor aspects of his arms. Which one of the following antibodies is most likely to be positive?

<input type="radio"/>	A. Anti-mitochondrial antibody
<input type="radio"/>	B. Anti-gliadin antibody
<input type="radio"/>	C. Anti-nuclear antibody
<input type="radio"/>	D. Anti-neutrophil cytoplasmic antibody
<input type="radio"/>	E. Anti-Jo-1 antibody

[Next question](#)

### Dermatitis herpetiformis

Dermatitis herpetiformis is an autoimmune blistering skin disorder associated with coeliac disease. It is caused by deposition of IgA in the dermis.

#### Features

- itchy, vesicular skin lesions on the extensor surfaces (e.g. elbows, knees buttocks)

#### Diagnosis

- skin biopsy: direct immunofluorescence shows deposition of IgA in a granular pattern in the upper dermis

#### Management

- gluten-free diet
- dapsone

**Question 52 of 129**

Next

A 65-year-old woman presents with bullae on her forearms following a recent holiday in Spain. She also notes that the skin on her hands is extremely fragile and tears easily. In the past the patient has been referred to dermatology due to troublesome hypertrichosis. What is the most likely diagnosis?

<input type="radio"/>	A. Pellagra
<input type="radio"/>	B. Pemphigus vulgaris
<input type="radio"/>	C. Epidermolysis bullosa
<input type="radio"/>	D. Bullous pemphigoid
<input type="radio"/>	E. Porphyria cutanea tarda

Next question

**Porphyria cutanea tarda**

- blistering photosensitive rash
- hypertrichosis
- hyperpigmentation

**Porphyria cutanea tarda**

Porphyria cutanea tarda is the most common hepatic porphyria. It is due to an inherited defect in uroporphyrinogen decarboxylase or caused by hepatocyte damage e.g. alcohol, oestrogens

**Features**

- classically presents with photosensitive rash with blistering and skin fragility on the face and dorsal aspect of hands (most common feature)
- hypertrichosis
- hyperpigmentation

**Investigations**

- urine: elevated uroporphyrinogen and pink fluorescence of urine under Wood's lamp

**Management**

- chloroquine
- venesection

A 34-year-old man comes for review. Over the past two weeks he has developed a number of painful, erythematous lesions on his shins. He has no dermatological history of note and is usually fit and well. On examination the lesions are consistent with erythema nodosum. You arrange some baseline investigations. He asks what is likely to happen. What is the most appropriate response?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Heal without scarring if steroids are given within 2 weeks |
| <input type="radio"/> | B. Heal without scarring within 6-12 months                   |
| <input type="radio"/> | C. Heal without scarring within 1-2 months                    |
| <input type="radio"/> | D. Heal with scarring within 1-2 months                       |
| <input type="radio"/> | E. Heal with scarring within 6-12 months                      |

[Next question](#)

## Erythema nodosum

### Overview

- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

### Causes

- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy



A 64-year-old woman presents with severe mucosal ulceration associated with the development of blistering lesions over her torso and arms. On examination the blisters are flaccid and easily ruptured when touched. What is the most likely diagnosis?

<input type="radio"/>	A. Pemphigus vulgaris
<input type="radio"/>	B. Pemphigoid
<input type="radio"/>	C. Dermatitis herpetiformis
<input type="radio"/>	D. Psoriasis
<input type="radio"/>	E. Epidermolysis bullosa

[Next question](#)

#### Blisters/bullae

- no mucosal involvement: bullous pemphigoid
- mucosal involvement: pemphigus vulgaris

### Pemphigus vulgaris

Pemphigus vulgaris is an autoimmune disease caused by antibodies directed against desmoglein, a cadherin-type epithelial cell adhesion molecule. It is more common in the Ashkenazi Jewish population

#### Features

- mucosal ulceration is common and often the presenting symptom. Oral involvement is seen in 50-70% of patients
- skin blistering - flaccid, easily ruptured vesicles and bullae. Lesions are typically painful but not itchy. These may develop months after the initial mucosal symptoms. Nikolsky's describes the spread of bullae following application of horizontal, tangential pressure to the skin
- acantholysis on biopsy

#### Management

- steroids
- immunosuppressants

A 17-year-old man presents with a 2 week history of abdominal pain, diarrhoea and repeated episodes of flushing. Examination reveals urticarial skin lesions on the trunk. What test is most likely to reveal the diagnosis?

<input type="radio"/>	A. Chest x-ray
<input type="radio"/>	B. Urinary catecholamines
<input type="radio"/>	C. Serum amylase
<input type="radio"/>	D. Urinary 5-HIAA
<input type="radio"/>	E. Urinary histamine

[Next question](#)

Urinary histamine is used to diagnose systemic mastocytosis

Given the history of diarrhoea and flushing a diagnosis of carcinoid syndrome should be considered, which would be investigated with urinary 5-HIAA levels. This would not however explain the urticarial skin lesions. In a young person a diagnosis of systemic mastocytosis should be considered. Another factor against carcinoid syndrome is the age of the patient - the average age of a patient with a carcinoid tumour is 61 years

### Systemic mastocytosis

Systemic mastocytosis results from a neoplastic proliferation of mast cells

#### Features

- urticaria pigmentosa - produces a wheal on rubbing (Darier's sign)
- flushing
- abdominal pain
- monocytosis on the blood film

#### Diagnosis

- raised serum tryptase levels
- urinary histamine

Which of the following skin conditions associated with malignancy are not correctly paired?

- ☐ A. Necrolytic migratory erythema and glucagonoma
- ☐ B. Migratory thrombophlebitis and pancreatic cancer
- ☐ C. Erythema gyratum repens and lymphoma
- ☐ D. Acanthosis nigricans and gastrointestinal cancer
- ☐ E. Erythroderma and lymphoma

Next question

Erythema gyratum repens is generally associated with solid organ malignancies such as lung and breast cancer

### Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	Associated malignancies
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Ovarian and lung cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

A 54-year-old man presents with a two month history of a rapidly growing lesion on his right forearm. The lesion initially appeared as a red papule but in the last two weeks has become a crater filled centrally with yellow/brown material. On examination the man has skin type II, the lesion is 4 mm in diameter and is morphologically as described above. What is the most likely diagnosis?

- |                                  |                          |
|----------------------------------|--------------------------|
| <input type="radio"/>            | A. Seborrhoeic keratosis |
| <input checked="" type="radio"/> | B. Keratoacanthoma       |
| <input type="radio"/>            | C. Pyoderma gangrenosum  |
| <input type="radio"/>            | D. Basal cell carcinoma  |
| <input type="radio"/>            | E. Malignant melanoma    |

[Next question](#)

### Keratoacanthoma

Keratoacanthoma is a benign epithelial tumour. They are more frequent in middle age and do not become more common in old age (unlike basal cell and squamous cell carcinoma)

Features - said to look like a volcano or crater

- initially a smooth dome-shaped papule
- rapidly grows to become a crater centrally-filled with keratin

Spontaneous regression of keratoacanthoma within 3 months is common, often resulting in a scar. Such lesions should however be urgently excised as it is difficult clinically to exclude squamous cell carcinoma. Removal also may prevent scarring

**Question 58 of 129**

Next

You review a 50-year-old man who has psoriasis. Which one of the following medications is most likely exacerbate his condition?

<input type="radio"/>	A. Nicorandil
<input type="radio"/>	B. Simvastatin
<input type="radio"/>	C. Verapamil
<input type="radio"/>	D. Atenolol
<input type="radio"/>	E. Isosorbide mononitrate

Next question

**Psoriasis: exacerbating factors**

The following factors may exacerbate psoriasis:

- trauma
- alcohol
- drugs: beta blockers, lithium, antimalarials (chloroquine and hydroxychloroquine), NSAIDs and ACE inhibitors
- withdrawal of systemic steroids

A 23-year-old man presents as he is concerned over recent hair loss. Examination reveals a discrete area of hair loss on the left temporal region with no obvious abnormality of the underlying scalp. What is the most likely diagnosis?

<input type="radio"/>	A. Telogen effluvium
<input type="radio"/>	B. Alopecia areata
<input type="radio"/>	C. Tinea capitis
<input type="radio"/>	D. Male-pattern baldness
<input type="radio"/>	E. Discoid lupus erythematosus

[Next question](#)

### Alopecia areata

Alopecia areata is a presumed autoimmune condition causing localised, well demarcated patches of hair loss. At the edge of the hair loss, there may be small, broken 'exclamation mark' hairs

Hair will regrow in 50% of patients by 1 year, and in 80-90% eventually. Careful explanation is therefore sufficient in many patients. Other treatment options include:

- topical or intralesional corticosteroids
- topical minoxidil
- phototherapy
- dithranol
- contact immunotherapy
- wigs

**Question 60 of 129**

Next

A 25-year-old male presents with extensive patches of altered pigmentation on his front, back, face and thighs. There is mild pruritus. A diagnosis of extensive pityriasis versicolor is made. What is the most appropriate management?

<input type="radio"/>	A. Oral metronidazole
<input type="radio"/>	B. Topical terbinafine
<input type="radio"/>	C. Oral itraconazole
<input type="radio"/>	D. Topical selenium sulphide
<input type="radio"/>	E. Oral terbinafine

Next question

Given the extensive nature of the lesions systemic therapy is indicated in this case

**Pityriasis versicolor**

Pityriasis versicolor, also called tinea versicolor, is a superficial cutaneous fungal infection caused by *Malassezia furfur* (formerly termed *Pityrosporum ovale*)

**Features**

- most commonly affects trunk
- patches may be hypopigmented, pink or brown (hence versicolor)
- scale is common
- mild pruritus

**Predisposing factors**

- occurs in healthy individuals
- immunosuppression
- malnutrition
- Cushing's

**Management**

- topical antifungal e.g. terbinafine or selenium sulphide
- if extensive disease or failure to respond to topical treatment then consider oral itraconazole

**Question 61 of 129**

Next

A 54-year-old woman with a history of type 1 diabetes mellitus presents with unsightly toenails affecting the lateral three nails of the left foot. On examination the nails are brown and break easily. Nail scrapings demonstrate *Trichophyton rubrum* infection. What is the treatment of choice?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Oral terbinafine for 12 weeks    |
| <input type="radio"/> | B. Oral itraconazole for 4 weeks    |
| <input type="radio"/> | C. Topical itraconazole for 2 weeks |
| <input type="radio"/> | D. Topical amorolfine for 6 weeks   |
| <input type="radio"/> | E. Oral itraconazole for 1 week     |

Next question

Dermatophyte nail infections - use oral terbinafine

**Fungal nail infections**

Onychomycosis is fungal infection of the nails. This may be caused by

- dermatophytes - mainly *Trichophyton rubrum*, accounts for 90% of cases
- yeasts - such as *Candida*
- non-dermatophyte moulds

**Features**

- 'unsightly' nails are a common reason for presentation
- thickened, rough, opaque nails are the most common finding

**Investigation**

- nail clippings
- scrapings of the affected nail

**Management**

- treatment is successful in around 50-80% of people
- diagnosis should be confirmed by microbiology before starting treatment



- dermatophyte infection: oral terbinafine is currently recommended first-line with oral itraconazole as an alternative. Six weeks - 3 months therapy is needed for fingernail infections whilst toenails should be treated for 3 - 6 months
- *Candida* infection: mild disease should be treated with topical antifungals (e.g. Amorolfine) whilst more severe infections should be treated with oral itraconazole for a period of 12 weeks

**Question 62 of 129**

Next

A 81-year-old man is investigated after he develops a number of itchy blisters on his trunk. A skin biopsy suggests a diagnosis bullous pemphigoid. This is most likely to be caused by antibodies directed against:

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Adherens                   |
| <input type="radio"/> | B. Desmoglein-3               |
| <input type="radio"/> | C. Hemidesmosomal BP antigens |
| <input type="radio"/> | D. Occludin-2                 |
| <input type="radio"/> | E. Desmoglein-1               |

Next question

**Bullous pemphigoid**

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include

- itchy, tense blisters typically around flexures
- the blisters usually heal without scarring
- mouth is usually spared\*

Skin biopsy

- immunofluorescence shows IgG and C3 at the dermoepidermal junction

Management

- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used

\*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

**Question 63 of 129**

Next

A 60-year-old woman presents with a swelling just proximal to the nail bed on the left ring finger. She has a history of osteoarthritis but is usually well. On examination a 4mm, firm dome-shaped swelling is seen. What is the most likely diagnosis?

<input type="radio"/>	A. Fibrokeratoma
<input type="radio"/>	B. Epidermoid cyst
<input type="radio"/>	C. Orf
<input type="radio"/>	D. Myxoid cyst
<input type="radio"/>	E. Rheumatoid nodule

Next question

**Myxoid cyst**

Myxoid cysts (also known as mucous cysts) are benign ganglion cysts usually found on the distal, dorsal aspect of the finger. There is usually osteoarthritis in the surrounding joint. They are more common in middle-aged women.

A 3-year-old girl is taken to her doctor due to a rash on the right upper arm. On examination multiple raised lesions of about 2 mm in diameter are seen. On close inspection a central dimple is present in the majority of lesions. What is the likely diagnosis?

<input type="radio"/>	A. Roseola infantum
<input type="radio"/>	B. Molluscum contagiosum
<input type="radio"/>	C. Kawasaki disease
<input type="radio"/>	D. Viral warts
<input type="radio"/>	E. Pityriasis rosea

[Next question](#)

### Molluscum contagiosum

Molluscum contagiosum is caused by a pox DNA virus infection. It is typically seen in younger children and results in characteristic small, pearly, umbilicated lesions

Molluscum contagiosum is highly infectious.

Lesions may be present for up to 12 months and usually resolve spontaneously. Whilst various treatments may be effective in removing the lesions (e.g. surgery, cryotherapy, topical agents) no treatment is recommended in the initial phase due to the benign nature of the condition

A 45-year-old man with a history of seborrhoeic dermatitis presents in late winter due a flare in his symptoms, affecting both his face and scalp. Which one of the following agents is least likely to be beneficial?

<input type="radio"/>	A. Topical ketoconazole
<input type="radio"/>	B. Selenium sulphide shampoo
<input type="radio"/>	C. Topical hydrocortisone
<input type="radio"/>	D. Tar shampoo
<input type="radio"/>	E. Aqueous cream

[Next question](#)

There is less of a role for emollients in the management of seborrhoeic dermatitis than in other chronic skin disorders

### Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called *Malassezia furfur* (formerly known as *Pityrosporum ovale*). It is common, affecting around 2% of the general population

#### Features

- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

#### Associated conditions include

- HIV
- Parkinson's disease

#### Scalp disease management

- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

#### Face and body management

- topical antifungals: e.g. Ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

A 48-year-old man with a history of psoriasis develops plaques on his face. Of the following options, which one is the most appropriate treatment?

<input type="radio"/>	A. Hydrocortisone 1%
<input type="radio"/>	B. Calcipotriol
<input type="radio"/>	C. Coal tar
<input type="radio"/>	D. Dithranol
<input type="radio"/>	E. Tacrolimus

Next question

Difficult question, particularly as there is an emphasis on patient-doctor choice when deciding upon treatment in psoriasis. Vitamin D analogues can be used in this situation but calcipotriol is not recommended as it may cause irritation - calcitriol and tacalcitol are alternatives. Mild potency topical steroids are useful for the management of facial psoriasis. Coal tar is smelly and messy - most patients would not tolerate facial application

### Psoriasis: management

SIGN released guidelines in 2010 on the management of psoriasis and psoriatic arthropathy. Please see the link for more details.

#### Chronic plaque psoriasis

- regular emollients may help to reduce scale loss and reduce pruritus
- for acute control SIGN recommend: 'Short term intermittent use of a potent topical corticosteroid or a combined potent corticosteroid plus calcipotriol

ointment is recommended to gain rapid improvement in plaque psoriasis.'

- 'For long term topical treatment of plaque psoriasis a vitamin D analogue (e.g. Calcipotriol) is recommended.'
- 'If a vitamin D analogue is ineffective or not tolerated then consider coal tar (solution, cream or lotion), tazarotene gel, or short contact dithranol (30 minute exposure in patients with a small number of relatively large plaques of psoriasis).

#### Steroids in psoriasis

- topical steroids are commonly used in flexural psoriasis and there is also a role for mild steroids in facial psoriasis. If steroids are ineffective for these conditions vitamin D analogues or tacrolimus ointment should be used second line
- SIGN caution against the long term use of potent or very potent topical steroids due to the risk of side-effects

## Scalp psoriasis

- for short term control SIGN recommend either the use of potent topical corticosteroids or a combination of a potent corticosteroid and a vitamin D

## analogue

- 'For patients with thick scaling of the scalp, initial treatment with overnight application of salicylic acid, tar preparations, or oil preparations (eg olive oil, coconut oil) to remove thick scale is recommended.

## Secondary care management

### Phototherapy

- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

### Systemic therapy

- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab
- ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials

### Mechanism of action of commonly used drugs:

- coal tar: probably inhibit DNA synthesis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

A 22-year-old male is referred to dermatology clinic with a longstanding problem of bilateral excessive axillary sweating. He is otherwise well but the condition is affecting his confidence and limiting his social life. What is the most appropriate management?

<input type="radio"/>	A. Non-sedating antihistamine
<input type="radio"/>	B. Topical hydrocortisone 1%
<input type="radio"/>	C. Perform thyroid function tests
<input type="radio"/>	D. Topical aluminium chloride
<input type="radio"/>	E. Trial of desmopressin

[Next question](#)

## Hyperhidrosis

Hyperhidrosis describes the excessive production of sweat

Management options include

- topical aluminium chloride preparations are first-line. Main side effect is skin irritation
- iontophoresis: particularly useful for patients with palmar, plantar and axillary hyperhidrosis
- botulinum toxin: currently licensed for axillary symptoms
- surgery: e.g. Endoscopic transthoracic sympathectomy. Patients should be made aware of the risk of compensatory sweating



A 23-year-old man presents with a 4 day history of an itchy and sore right ear. He has recently returned from holiday in Spain. On examination the right ear canal is inflamed but no debris is seen. The tympanic membrane is clearly visible and is unremarkable. What is the most appropriate management?

<input type="radio"/>	A. Topical corticosteroid + aminoglycoside
<input type="radio"/>	B. Topical corticosteroid
<input type="radio"/>	C. Refer to ENT
<input type="radio"/>	D. Topical corticosteroid + clotrimazole
<input type="radio"/>	E. Oral flucloxacillin

[Next question](#)

This patient has otitis externa, which commonly develops after swimming on holiday. The first line management is either a topical antibiotic or a combined topical antibiotic and steroid.

### Otitis externa

Otitis externa is a common reason for primary care attendance in the UK.

Causes of otitis externa include:

- infection: bacterial (*Staphylococcus aureus*, *Pseudomonas aeruginosa*) or fungal
- seborrhoeic dermatitis
- contact dermatitis (allergic and irritant)

### Features

- ear pain, itch, discharge
- otoscopy: red, swollen, or eczematous canal

The recommend initial management of otitis externa is:

- topical antibiotic or a combined topical antibiotic with steroid
- if the tympanic membrane is perforated aminoglycosides are traditionally not used\*
- if there is canal debris then consider removal
- if the canal is extensively swollen then an ear wick is sometimes inserted

Second line options include

- consider contact dermatitis secondary to neomycin
- oral antibiotics if the infection is spreading

- taking a swab inside the ear canal
- empirical use of an antifungal agent

Malignant otitis externa is more common in elderly diabetics. In this condition there is extension of infection into the bony ear canal and the soft tissues deep to the bony canal. Intravenous antibiotics may be required.

\*many ENT doctors disagree with this and feel that concerns about ototoxicity are unfounded

A 29-year-old man consults you regarding a rash he has noticed around his groin. It has been present for the past 3 months and is asymptomatic. On examination there is a symmetrical well-demarcated, brown-red macular rash around the groin. What is the most likely diagnosis?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Erythrasma                 |
| <input type="radio"/> | B. Pityriasis versicolor      |
| <input type="radio"/> | C. Secondary syphilis         |
| <input type="radio"/> | D. Acanthosis nigricans       |
| <input type="radio"/> | E. <i>Candidal</i> intertrigo |

[Next question](#)

### Erythrasma

Erythrasma is a generally asymptomatic, flat, slightly scaly, pink or brown rash usually found in the groin or axillae. It is caused by an overgrowth of the diphtheroid *Corynebacterium minutissimum*.

Examination with Wood's light reveals a coral-red fluorescence.

Topical miconazole or antibacterial are usually effective. Oral erythromycin may be used for more extensive infection.

Which one of the following conditions is least associated with photosensitivity?

<input type="radio"/>	A. Discoid lupus erythematosus
<input type="radio"/>	B. Systemic lupus erythematosus
<input type="radio"/>	C. Herpes labialis
<input type="radio"/>	D. Acute intermittent porphyria
<input type="radio"/>	E. Xeroderma pigmentosum

Next question

Photosensitivity is not a feature of acute intermittent porphyria unlike porphyria cutanea tarda

### Photosensitive skin disorders

Diseases aggravated by exposure to sunlight

- systemic lupus erythematosus, discoid lupus
- porphyria (not acute intermittent)
- herpes labialis (cold sores)
- pellagra
- xeroderma pigmentosum
- solar urticaria
- polymorphic light eruption

**Question 71 of 129**

Next

A 15-year-old girl presents with an urticarial rash, angioedema and wheezing. Her mother states that she has just come from her younger sister's party where she had been helping to blow up balloons. What is the most likely diagnosis?

<input type="radio"/>	A. C1-esterase deficiency (hereditary angioedema)
<input type="radio"/>	B. Allergic contact dermatitis
<input type="radio"/>	C. Peanut allergy
<input type="radio"/>	D. Latex allergy
<input type="radio"/>	E. Irritant contact dermatitis

Next question

This is a typical history of latex allergy. Adrenaline should be given immediately and usual anaphylaxis management followed

**Hypersensitivity**

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

**Type I - Anaphylactic**

- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

**Type II - Cell bound**

- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

**Type III - Immune complex**

- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

**Type IV - Delayed hypersensitivity**

- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

Type V - Stimulated hypersensitivity

- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis

A 72-year-old woman is diagnosed with a number of erythematous, rough lesions on the back of her hands. A diagnosis of actinic keratoses is made. What is the most appropriate management?

<input type="radio"/>	A. Reassurance
<input type="radio"/>	B. Urgent referral to a dermatologist
<input type="radio"/>	C. Topical fluorouracil cream
<input type="radio"/>	D. Review in 3 months
<input type="radio"/>	E. Topical betnovate

[Next question](#)

### Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

#### Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

#### Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

An 84-year-old woman with a history of ischaemic heart disease is reviewed in the dermatology clinic. Her current medication includes aspirin, simvastatin, bisoprolol, ramipril and isosorbide mononitrate. She has developed tense blistering lesions on her legs. Each lesion is around 1 to 3 cm in diameter and she reports that they are slightly pruritic. Examination of her mouth and vulva is unremarkable. What is the most likely diagnosis?

- ☐ A. Pemphigus
- ☐ B. Drug reaction to aspirin
- ☐ C. Epidermolysis bullosa
- ☐ D. Scabies
- ☐ E. Bullous pemphigoid

[Next question](#)

#### Blisters/bullae

- no mucosal involvement (in exams at least\*): bullous pemphigoid
- mucosal involvement: pemphigus vulgaris

### Bullous pemphigoid

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include

- itchy, tense blisters typically around flexures
- the blisters usually heal without scarring
- mouth is usually spared\*

#### Skin biopsy

- immunofluorescence shows IgG and C3 at the dermoepidermal junction

#### Management

- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used



\*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

A 29-year-old man presents due to the development of 'hard skin' on his scalp. On examination he has a 9cm circular, white, hyperkeratotic lesion on the crown of his head. He has no past history of any skin or scalp disorder. Skin scrapings are reported as follows:

No fungal elements seen

What is the most likely diagnosis?

<input type="radio"/>	A. Psoriasis
<input type="radio"/>	B. Dissecting cellulitis
<input type="radio"/>	C. Kerion
<input type="radio"/>	D. Systemic lupus erythematosus
<input type="radio"/>	E. Seborrhoeic dermatitis

Next question

As the skin scraping is negative for fungi the most likely diagnosis is psoriasis. Scalp psoriasis may occur in isolation in patients with no history of psoriasis elsewhere. Please see the link for more information.

The white appearance of the lesion is secondary to the 'silver scale' covering the psoriatic plaque.

## Psoriasis

Psoriasis is a common and chronic skin disorder. It generally presents with red, scaly patches on the skin although it is now recognised that patients with psoriasis are at increased risk of arthritis and cardiovascular disease.

### Pathophysiology

- multifactorial and not yet fully understood
- genetic: associated HLA-B13, -B17, and -Cw6. Strong concordance (70%) in identical twins
- immunological: abnormal T cell activity stimulates keratinocyte proliferation. There is increasing evidence this may be mediated by a novel group of T helper cells producing IL-17, designated Th17. These cells seem to be a third T-effector cell subset in addition to Th1 and Th2
- environmental: it is recognised that psoriasis may be worsened (e.g. Skin trauma, stress), triggered (e.g. Streptococcal infection) or improved (e.g. Sunlight) by environmental factors

### Recognised subtypes of psoriasis

- plaque psoriasis: the most common sub-type resulting in the typical well demarcated red, scaly patches affecting the extensor surfaces, sacrum and scalp
- flexural psoriasis: in contrast to plaque psoriasis the skin is smooth

- guttate psoriasis: transient psoriatic rash frequently triggered by a streptococcal infection. Multiple red, teardrop lesions appear on the body
- pustular psoriasis: commonly occurs on the palms and soles

#### Other features

- nail signs: pitting, onycholysis
- arthritis

#### Complications

- psoriatic arthropathy (around 10%)
- increased incidence of metabolic syndrome
- increased incidence of cardiovascular disease
- psychological distress

A 15-year-old male returns to the dermatology clinic for review. He has a past history of acne and is currently treated with oral lymecycline. There has been no response to treatment and examination reveals evidence of scarring on his face. What is the most suitable treatment?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Oral doxycycline         |
| <input type="radio"/> | B. Oral cyproterone acetate |
| <input type="radio"/> | C. Oral isotretinoin        |
| <input type="radio"/> | D. IV retinoin              |
| <input type="radio"/> | E. Topical retinoids        |

[Next question](#)

### Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicles with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. Oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Each one of the following is associated with yellow nail syndrome except:

<input type="radio"/>	A. Chronic sinus infections
<input type="radio"/>	B. Bronchiectasis
<input type="radio"/>	C. Azoospermia
<input type="radio"/>	D. Congenital lymphoedema
<input type="radio"/>	E. Pleural effusions

Next question

### Yellow nail syndrome

Slowing of the nail growth leads to the characteristic thickened and discoloured nails seen in yellow nail syndrome.

#### Associations

- congenital lymphoedema
- pleural effusions
- bronchiectasis
- chronic sinus infections

A 54-year-old woman is prescribed topical fusidic acid for a small patch of impetigo around her nose. She has recently been discharged from hospital following varicose vein surgery. Seven days after starting treatment there has been no change in her symptoms. Examination reveals a persistent small, crusted area around the right nostril. Whilst awaiting the results of swabs, what is the most appropriate management?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Oral vancomycin       |
| <input type="radio"/> | B. Oral erythromycin     |
| <input type="radio"/> | C. Topical metronidazole |
| <input type="radio"/> | D. Topical mupirocin     |
| <input type="radio"/> | E. Oral flucloxacillin   |

[Next question](#)

MRSA should be considered given the recent hospital stay and lack of response to fusidic acid. Topical mupirocin is therefore the most appropriate treatment.

### Impetigo: management

Limited, localised disease

- topical fusidic acid is first-line
- topical retapamulin is used second-line if fusidic acid has been ineffective or is not tolerated
- MRSA is not susceptible to either fusidic acid or retapamulin. Topical mupirocin (Bactroban) should therefore be used in this situation

Extensive disease

- oral flucloxacillin
- oral erythromycin if penicillin allergic

Café-au-lait spots are seen in each of the following, except:

<input type="radio"/>	A. McCune-Albright syndrome
<input type="radio"/>	B. Friedreich's ataxia
<input type="radio"/>	C. Neurofibromatosis
<input type="radio"/>	D. Fanconi anaemia
<input type="radio"/>	E. Tuberous sclerosis

Next question

### Café-au-lait spots

Hyperpigmented lesions that vary in colour from light brown to dark brown, with borders that may be smooth or irregular

#### Causes

- neurofibromatosis type I & II
- tuberous sclerosis
- Fanconi anaemia
- McCune-Albright syndrome

A 43-year-old presents with itchy lesions on the soles of both feet. These have been present for the past two months. On examination small blisters are seen with surrounding dry and cracked skin. What is the most likely diagnosis?

<input type="radio"/>	A. Porphyria cutanea tarda
<input type="radio"/>	B. Pustular psoriasis
<input type="radio"/>	C. Pompholyx
<input type="radio"/>	D. Bullous pemphigoid
<input type="radio"/>	E. Pemphigus

[Next question](#)

## Pompholyx

Pompholyx is a type of eczema which affects both the hands (cheiropompholyx) and the feet (pedopompholyx). It is also known as dyshidrotic eczema

### Features

- small blisters on the palms and soles
- pruritic, sometimes burning sensation
- once blisters burst skin may become dry and crack

### Management

- cool compresses
- emollients
- topical steroids



A 45-year-old woman is presents with itchy, violaceous papules on the flexor aspects of her wrists. She is normally fit and well and has not had a similar rash previously. Given the likely diagnosis, what other feature is she most likely to have?

<input type="radio"/>	A. Onycholysis
<input type="radio"/>	B. Raised ESR
<input type="radio"/>	C. Mucous membrane involvement
<input type="radio"/>	D. Pain in small joints
<input type="radio"/>	E. Microscopic haematuria

Next question

### Lichen

- **planus**: **p**urple, **p**ruritic, **p**apular, **p**olygonal rash on flexor surfaces. Wickham's striae over surface. Oral involvement common
- **sclerosus**: itchy white spots typically seen on the vulva of elderly women

Mucous membrane involvement is common in lichen planus

### Lichen planus

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

### Features

- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon may be seen (new skin lesions appearing at the site of trauma)
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:

- gold
- quinine
- thiazides

### Management

- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

A 9-year-old child with a history of atopic eczema presents with a sudden worsening of her skin. Her eczema is usually well controlled with emollients but her parents are concerned as the facial eczema has got significantly worse overnight. She now has painful clustered blisters on both cheeks, around her mouth on her neck. Her temperature is 37.9°C. What is the most appropriate management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Advise paracetamol + emollients and reassure |
| <input type="radio"/> | B. Intravenous aciclovir                        |
| <input type="radio"/> | C. Potent topical steroid                       |
| <input type="radio"/> | D. Intravenous flucloxacillin                   |
| <input type="radio"/> | E. Oral fluconazole                             |

[Next question](#)

### Eczema herpeticum

Eczema herpeticum describes a severe primary infection of the skin by herpes simplex virus 1 or 2. It is more commonly seen in children with atopic eczema. As it is potentially life threatening children should be admitted for IV aciclovir

A woman presents with painful erythematous lesions on her shins. Which one of the following is least associated with this presentation?

<input type="radio"/>	A. Pregnancy
<input type="radio"/>	B. Behcet's syndrome
<input type="radio"/>	C. Streptococcal infection
<input type="radio"/>	D. Penicillin
<input type="radio"/>	E. Amyloidosis

[Next question](#)

## Erythema nodosum

### Overview

- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

### Causes

- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

**Question 83 of 129**

Next

A 34-year-old female is reviewed in the dermatology clinic with a skin rash under her new wrist watch. An allergy to nickel is suspected. What is the best investigation?

<input type="radio"/>	A. Skin prick test
<input type="radio"/>	B. Skin patch test
<input type="radio"/>	C. Skin biopsy
<input type="radio"/>	D. Serum IgE
<input type="radio"/>	E. Serum nickel antibodies

Next question

**Nickel dermatitis**

Nickel is a common cause allergic contact dermatitis and is an example of a type IV hypersensitivity reaction. It is often caused by jewellery such as watches

It is diagnosed by a skin patch test

A 43-year-old woman is referred to psychiatry following repeated episodes of hypomaniac behaviour interspersed with periods of depression. Her past medical history includes psoriasis and a deep vein thrombosis 11 years ago. Which one of the following medications is most likely to worsen her psoriasis?

- |                       |                     |
|-----------------------|---------------------|
| <input type="radio"/> | A. Sodium valproate |
| <input type="radio"/> | B. Quetiapine       |
| <input type="radio"/> | C. Lithium          |
| <input type="radio"/> | D. Valproaic acid   |
| <input type="radio"/> | E. Fluoxetine       |

[Next question](#)

Psoriasis: common triggers are beta-blockers and lithium

### Psoriasis: exacerbating factors

The following factors may exacerbate psoriasis:

- trauma
- alcohol
- drugs: beta blockers, lithium, antimalarials (chloroquine and hydroxychloroquine), NSAIDs and ACE inhibitors
- withdrawal of systemic steroids

A 20-year-old man presents with acute gingivitis associated with oral ulceration. A diagnosis of primary herpes simplex infection is suspected. Which one of the following types of rash is he most likely to go on to develop?

<input type="radio"/>	A. Erythema ab igne
<input type="radio"/>	B. Erythema nodosum
<input type="radio"/>	C. Erythema chronicum migrans
<input type="radio"/>	D. Erythema marginatum
<input type="radio"/>	E. Erythema multiforme

[Next question](#)

## Erythema multiforme

### Features

- target lesions
- initially seen on the back of the hands / feet before spreading to the torso
- upper limbs are more commonly affected than the lower limbs
- pruritus is occasionally seen and is usually mild

If symptoms are severe and involve blistering and mucosal involvement the term Stevens-Johnson syndrome is used.

### Causes

- viruses: herpes simplex virus (the most common cause), Orf\*
- idiopathic
- bacteria: *Mycoplasma*, *Streptococcus*
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill, nevirapine
- connective tissue disease e.g. Systemic lupus erythematosus
- sarcoidosis
- malignancy

\*Orf is a skin disease of sheep and goats caused by a parapox virus

A 17-year-old female originally from Nigeria presents due to a swelling around her earlobe. She had her ears pierced around three months ago and has noticed the gradual development of an erythematous swelling since. On examination a keloid scar is seen. What is the most appropriate management?

<input type="radio"/>	A. Intralesional diclofenac
<input type="radio"/>	B. Advise no treatment is available
<input type="radio"/>	C. Intralesional triamcinolone
<input type="radio"/>	D. Advise will spontaneously regress within 4-6 months
<input type="radio"/>	E. Intralesional sclerotherapy

[Next question](#)

### Keloid scars

Keloid scars are tumour-like lesions that arise from the connective tissue of a scar and extend beyond the dimensions of the original wound

#### Predisposing factors

- ethnicity: more common in people with dark skin
- occur more commonly in young adults, rare in the elderly
- common sites (in order of decreasing frequency): sternum, shoulder, neck, face, extensor surface of limbs, trunk

Keloid scars are less likely if incisions are made along relaxed skin tension lines\*

#### Treatment

- early keloids may be treated with intra-lesional steroids e.g. triamcinolone
- excision is sometimes required

\*Langer lines were historically used to determine the optimal incision line. They were based on procedures done on cadavers but have been shown to produce worse cosmetic results than when following skin tension lines

A 58-year-old woman presents with a persistent erythematous rash on her cheeks and a 'red nose'. She describes occasional episodes of facial flushing. On examination erythematous skin is noted on the nose and cheeks associated with occasional telangiectasia. What is the most appropriate management?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Topical metronidazole  |
| <input type="radio"/> | B. Topical isotretinoin   |
| <input type="radio"/> | C. Benzyl peroxide        |
| <input type="radio"/> | D. Daktacort              |
| <input type="radio"/> | E. Topical hydrocortisone |

[Next question](#)

Acne rosacea treatment:

- mild/moderate: topical metronidazole
- severe/resistant: oral tetracycline

Given that this woman has mild symptoms, topical metronidazole should be used first line

### Acne rosacea

Acne rosacea is a chronic skin disease of unknown aetiology

#### Features

- typically affects nose, cheeks and forehead
- flushing is often first symptom
- telangiectasia are common
- later develops into persistent erythema with papules and pustules
- rhinophyma
- ocular involvement: blepharitis

#### Management

- topical metronidazole may be used for mild symptoms (i.e. Limited number of papules and pustules, no plaques)
- more severe disease is treated with systemic antibiotics e.g. Oxytetracycline
- recommend daily application of a high-factor sunscreen
- camouflage creams may help conceal redness
- laser therapy may be appropriate for patients with prominent telangiectasia



A 78-year-old nursing home resident is reviewed due to the development of an intensely itchy rash. On examination red linear lesions are seen on the wrists and elbows, and red papules are present on the penis. What is the most appropriate management?

<input type="radio"/>	A. Topical permethrin
<input type="radio"/>	B. Referral to GUM clinic
<input type="radio"/>	C. Topical betnovate
<input type="radio"/>	D. Topical ketoconazole
<input type="radio"/>	E. Topical selenium sulphide

[Next question](#)

Lichen planus may give a similar picture but the intense itching is more characteristic of scabies. It is also less common for lichen planus to present in the elderly - it typically affects patients aged 30-60 years.

## Scabies

Scabies is caused by the mite *Sarcoptes scabiei* and is spread by prolonged skin contact. It typically affects children and young adults.

The scabies mite burrows into the skin, laying its eggs in the stratum corneum. The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

### Features

- widespread pruritus
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

### Management

- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication

### Patient guidance on treatment (from Clinical Knowledge Summaries)

- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic

- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation. Patients should be given the following instructions:

- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8-12 hours for permethrin, or for 24 hours for malathion, before washing off
- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

A 63-year-old man who is known to have type 2 diabetes mellitus presents with a number of lesions over his shins. On examination there are a number of 3-4 mm smooth, firm, papules which are hyperpigmented and centrally depressed. What is the most likely diagnosis?

<input type="radio"/>	A. Lupus vulgaris
<input type="radio"/>	B. Necrobiosis lipoidica diabetorum
<input type="radio"/>	C. Guttate psoriasis
<input checked="" type="radio"/>	D. Granuloma annulare
<input type="radio"/>	E. Pyoderma gangrenosum

[Next question](#)

## Granuloma annulare

### Basics

- papular lesions that are often slightly hyperpigmented and depressed centrally
- typically occur on the dorsal surfaces of the hands and feet, and on the extensor aspects of the arms and legs

A number of associations have been proposed to conditions such as diabetes mellitus but there is only weak evidence for this

**Question 90 of 129**

Next

A 50-year-old chronic alcoholic presents with a persistent skin rash on his hands, arms, neck and face. The rash is red-brown in colour, symmetrical and scaly. He also complains of a poor appetite, nausea and diarrhoea.

Which vitamin deficiency is most likely to have caused his symptoms?

<input type="radio"/>	A. Niacin
<input type="radio"/>	B. Folic acid
<input type="radio"/>	C. Thiamine
<input type="radio"/>	D. Vitamin B6
<input type="radio"/>	E. Zinc

Next question

**Pellagra**

Pellagra is caused by nicotinic acid (niacin) deficiency. The classical features are the 3 D's - dermatitis, diarrhoea and dementia

Pellagra may occur as a consequence of isoniazid therapy (isoniazid inhibits the conversion of tryptophan to niacin) and it is more common in alcoholics.

**Features**

- dermatitis (brown scaly rash on sun-exposed sites - termed Casal's necklace if around neck)
- diarrhoea
- dementia, depression
- death if not treated

A 34-year-old man with a history of polyarthralgia, back pain and diarrhoea is found to have a 3 cm red lesion on his shin which is starting to ulcerate. What is the most likely diagnosis?

<input type="radio"/>	A. Systemic <i>Shigella</i> infection
<input type="radio"/>	B. Syphilis
<input type="radio"/>	C. Metastatic colon cancer
<input type="radio"/>	D. Erythema nodosum
<input type="radio"/>	E. Pyoderma gangrenosum

[Next question](#)

This patient is likely to have ulcerative colitis, which has a known association with large-joint arthritis, sacroilitis and pyoderma gangrenosum

### Pyoderma gangrenosum

#### Features

- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

#### Causes\*

- idiopathic in 50%
- inflammatory bowel disease: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

#### Management

- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

\*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

**Question 92 of 129**

Next

A 33-year-old is investigated for lethargy. The full blood count is reported as follows:

Hb	10.1 g/dl
Plt	$156 \times 10^9/l$
WBC	$3.7 \times 10^9/l$

His daughter was unwell one week previously with a pyrexial illness associated with a red rash on her cheeks. What is the most likely cause?

- ☐ A. Measles
- ☐ B. Coxsackie a16
- ☐ C. Group A haemolytic streptococci
- ☒ D. Parvovirus B19
- ☐ E. HHV-6 (Human Herpesvirus-6)

Next question

**Parvovirus B19**

Parvovirus B19 is a DNA virus which causes a variety of clinical presentations. It was identified in the 1980's as the cause of erythema infectiosum

Erythema infectiosum (also known as fifth disease or 'slapped-cheek syndrome')

- most common presenting illness
- systemic symptoms: lethargy, fever, headache
- 'slapped-cheek' rash spreading to proximal arms and extensor surfaces

Other presentations

- asymptomatic
- pancytopenia in immunosuppressed patients
- aplastic crises e.g. in sickle-cell disease (parvovirus B19 suppresses erythropoiesis for about a week so aplastic anaemia is rare unless there is a chronic haemolytic anaemia)

Which one of the following is least likely to cause a bullous rash?

<input type="radio"/>	A. Furosemide
<input type="radio"/>	B. Friction
<input type="radio"/>	C. Lichen planus
<input type="radio"/>	D. Insect bite
<input type="radio"/>	E. Epidermolysis bullosa

Next question

The bullous variant of lichen planus is extremely rare

### Bullous disorders

Causes of skin bullae

- congenital: epidermolysis bullosa
- autoimmune: bullous pemphigoid, pemphigus
- insect bite
- trauma/friction
- drugs: barbiturates, furosemide

A 64-year-old female is referred to dermatology due to a non-healing skin ulcer on her lower leg. This has been present for around 6 weeks and the appearance didn't improve following a course of oral flucloxacillin. What is the most important investigation to perform first?

<input type="radio"/>	A. MRI
<input type="radio"/>	B. Rheumatoid factor titres
<input type="radio"/>	C. Ankle-brachial pressure index
<input type="radio"/>	D. Swab of ulcer for culture and sensitivity
<input type="radio"/>	E. X-ray

[Next question](#)

An ankle-brachial pressure index measurement would help exclude arterial insufficiency as a contributing factor. If this was abnormal then a referral to the vascular surgeons should be considered.

If the ulcer fails to heal with active management (e.g. Compression bandaging) then referral for consideration of biopsy to exclude a malignancy should be made.

Ongoing infection is not a common cause of non-healing leg ulcers.

### Venous ulceration

Venous ulceration is typically seen above the medial malleolus

#### Investigations

- ankle-brachial pressure index (ABPI) is important in non-healing ulcers to assess for poor arterial flow which could impair healing
- a 'normal' ABPI may be regarded as between 0.9 - 1.2. Values below 0.9 indicate arterial disease. Interestingly, values above 1.3 may also indicate arterial disease, in the form of false-negative results secondary to arterial calcification (e.g. In diabetics)

#### Management

- compression bandaging, usually four layer (only treatment shown to be of real benefit)
- oral pentoxifylline, a peripheral vasodilator, improves healing rate
- small evidence base supporting use of flavinoids
- little evidence to suggest benefit from hydrocolloid dressings, topical growth factors, ultrasound therapy and intermittent pneumatic compression



A 33-year-old woman is reviewed in the dermatology clinic with patchy, well demarcated hair loss on the scalp. This is affecting around 20% of her total scalp, and causing significant psychological distress. A diagnosis of alopecia areata is suspected. Which one of the following is an appropriate management plan?

<input type="radio"/>	A. Topical 5-FU cream
<input type="radio"/>	B. Autoimmune screen
<input type="radio"/>	C. Topical ketoconazole
<input type="radio"/>	D. Topical corticosteroid
<input type="radio"/>	E. Autoimmune screen + topical ketoconazole

[Next question](#)

Watchful waiting for spontaneous remission is another option. Neither the British Association of Dermatologists or Clinical Knowledge Summaries recommend screening for autoimmune disease

### Alopecia areata

Alopecia areata is a presumed autoimmune condition causing localised, well demarcated patches of hair loss. At the edge of the hair loss, there may be small, broken 'exclamation mark' hairs

Hair will regrow in 50% of patients by 1 year, and in 80-90% eventually. Careful explanation is therefore sufficient in many patients. Other treatment options include:

- topical or intralesional corticosteroids
- topical minoxidil
- phototherapy
- dithranol
- contact immunotherapy
- wigs

A 17-year-old female presents with multiple comedones, pustules and papules on her face. Which one of the following is least likely to improve her condition?

<input type="radio"/>	A. Topical retinoids
<input type="radio"/>	B. Dietary advice
<input type="radio"/>	C. Sunlight
<input type="radio"/>	D. Oral trimethoprim
<input type="radio"/>	E. Ethinylestradiol with cyproterone acetate

[Next question](#)

There is no role for dietary modification in patients with acne vulgaris. Ethinylestradiol with cyproterone acetate (Dianette) is useful in some female patients with acne unresponsive to standard treatment. Oral trimethoprim is useful in patients on long-term antibiotics who develop Gram negative folliculitis

### Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicles with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. Oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

Each of the following drugs may be used in psoriasis, except:

<input type="radio"/>	A. Interferon alpha
<input type="radio"/>	B. Infliximab
<input type="radio"/>	C. Retinoids
<input type="radio"/>	D. Methotrexate
<input type="radio"/>	E. Ciclosporin

Next question

## Psoriasis: management

SIGN released guidelines in 2010 on the management of psoriasis and psoriatic arthropathy. Please see the link for more details.

### Chronic plaque psoriasis

- regular emollients may help to reduce scale loss and reduce pruritus
- for acute control SIGN recommend: 'Short term intermittent use of a potent topical corticosteroid or a combined potent corticosteroid plus calcipotriol

ointment is recommended to gain rapid improvement in plaque psoriasis.'

- 'For long term topical treatment of plaque psoriasis a vitamin D analogue (e.g. Calcipotriol) is recommended.'
- 'If a vitamin D analogue is ineffective or not tolerated then consider coal tar (solution, cream or lotion), tazarotene gel, or short contact dithranol (30 minute exposure in patients with a small number of relatively large plaques of psoriasis).

### Steroids in psoriasis

- topical steroids are commonly used in flexural psoriasis and there is also a role for mild steroids in facial psoriasis. If steroids are ineffective for these conditions vitamin D analogues or tacrolimus ointment should be used second line
- SIGN caution against the long term use of potent or very potent topical steroids due to the risk of side-effects

### Scalp psoriasis

- for short term control SIGN recommend either the use of potent topical corticosteroids or a combination of a potent corticosteroid and a vitamin D

analogue

- 'For patients with thick scaling of the scalp, initial treatment with overnight application of salicylic acid, tar preparations, or oil preparations (eg olive oil, coconut oil) to remove thick scale is recommended.

## Secondary care management

Phototherapy

- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

Systemic therapy

- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab
- ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials

Mechanism of action of commonly used drugs:

- coal tar: probably inhibit DNA synthesis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

**Question 98 of 129**

Next

A 34-year-old female with a history of discoid lupus erythematosus is reviewed in clinic. The erythematous, scaly rash on her face has not responded to topical steroid creams. What is the most appropriate next step in management?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. UV light therapy           |
| <input type="radio"/> | B. Oral hydroxychloroquine    |
| <input type="radio"/> | C. Topical dapsone            |
| <input type="radio"/> | D. Oral prednisolone          |
| <input type="radio"/> | E. Topical hydroxychloroquine |

Next question

Discoid lupus erythematosus - topical steroids --> oral hydroxychloroquine

**Discoid lupus erythematosus**

Discoid lupus erythematosus is a benign disorder generally seen in younger females. It very rarely progresses to systemic lupus erythematosus (in less than 5% of cases). Discoid lupus erythematosus is characterised by follicular keratin plugs and is thought to be autoimmune in aetiology

**Features**

- erythematous, raised rash, sometimes scaly
- may be photosensitive
- more common on face, neck, ears and scalp
- lesions heal with atrophy, scarring (may cause scarring alopecia), and pigmentation

**Management**

- topical steroid cream
- oral antimalarials may be used second-line e.g. hydroxychloroquine
- avoid sun exposure

### Question 99 of 129

Next

A 35-year-old female presents tender, erythematous nodules over her forearms. Blood tests reveal:

Calcium	2.78 mmol/l
---------	-------------

What is the most likely diagnosis?

- |                                  |                          |
|----------------------------------|--------------------------|
| <input type="radio"/>            | A. Granuloma annulare    |
| <input checked="" type="radio"/> | B. Erythema nodosum      |
| <input type="radio"/>            | C. Lupus pernio          |
| <input type="radio"/>            | D. Erythema multiforme   |
| <input type="radio"/>            | E. Necrobiosis lipoidica |

Next question

The likely underlying diagnosis is sarcoidosis

### Erythema nodosum

#### Overview

- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

#### Causes

- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy

A 62-year-old woman mentions in diabetes clinic that she has a 'volcano' like spot on her left cheek, which has appeared over the past 3 months. She initially thought it may be a simple spot but it has not gone away. On examination she has a 5 mm red, raised lesion with a central keratin filled crater. A clinical diagnosis of probable keratoacanthoma is made. What is the most suitable management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Reassure will spontaneously involute within 3 months |
| <input type="radio"/> | B. Urgent referral to dermatology                       |
| <input type="radio"/> | C. Topical 5-FU   |
| <input type="radio"/> | D. Non-urgent referral to dermatology                   |
| <input type="radio"/> | E. Oral prednisolone                                    |

[Next question](#)

Whilst keratoacanthoma is a benign lesion it is difficult clinically to exclude squamous cell carcinoma so urgent excision is advised

### Keratoacanthoma

Keratoacanthoma is a benign epithelial tumour. They are more frequent in middle age and do not become more common in old age (unlike basal cell and squamous cell carcinoma)

Features - said to look like a volcano or crater

- initially a smooth dome-shaped papule
- rapidly grows to become a crater centrally-filled with keratin

Spontaneous regression of keratoacanthoma within 3 months is common, often resulting in a scar. Such lesions should however be urgently excised as it is difficult clinically to exclude squamous cell carcinoma. Removal also may prevent scarring

A 74-year-old woman develops tense, itchy blisters on her inner thighs and upper arms. Given the likely diagnosis, what will immunofluorescence of the skin biopsy demonstrate?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Loss of fibrinogen at the basement membrane        |
| <input type="radio"/> | B. Granular IgG along the basement membrane           |
| <input type="radio"/> | C. IgM crystallization at the dermal junctions        |
| <input type="radio"/> | D. Linear IgA deposits at the dermoepidermal junction |
| <input type="radio"/> | E. IgG and C3 at the dermoepidermal junction          |

[Next question](#)

### Bullous pemphigoid

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include

- itchy, tense blisters typically around flexures
- the blisters usually heal without scarring
- mouth is usually spared\*

Skin biopsy

- immunofluorescence shows IgG and C3 at the dermoepidermal junction

Management

- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used

\*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.



**Question 102 of 129**

Next

A patient who is suspected of having dermatitis herpetiformis undergoes a skin biopsy. Which one of the following antibodies is most likely to be found in the dermis?

<input type="radio"/>	A. IgM
<input checked="" type="radio"/>	B. IgA
<input type="radio"/>	C. IgD
<input type="radio"/>	D. IgE
<input type="radio"/>	E. IgG

Next question

Dermatitis herpetiformis - caused by IgA deposition in the dermis

**Dermatitis herpetiformis**

Dermatitis herpetiformis is an autoimmune blistering skin disorder associated with coeliac disease. It is caused by deposition of IgA in the dermis.

**Features**

- itchy, vesicular skin lesions on the extensor surfaces (e.g. elbows, knees buttocks)

**Diagnosis**

- skin biopsy: direct immunofluorescence shows deposition of IgA in a granular pattern in the upper dermis

**Management**

- gluten-free diet
- dapsone

A 31-year-old female with polycystic ovarian syndrome consults you as she is troubled with excessive facial hair. Switching her combined oral contraceptive pill to co-cyprindiol has had no effect. On examination she has hirsutism affecting her moustache, beard, and temple areas. What is the most appropriate treatment?

<input type="radio"/>	A. Topical salicylic acid
<input type="radio"/>	B. Topical adapalene
<input type="radio"/>	C. Oral clomifene
<input type="radio"/>	D. Topical eflornithine
<input type="radio"/>	E. Topical tazarotene

[Next question](#)

### Polycystic ovarian syndrome: management

Polycystic ovarian syndrome (PCOS) is a complex condition of ovarian dysfunction thought to affect between 5-20% of women of reproductive age. Management is complicated and problem based partly because the aetiology of PCOS is not fully understood. Both hyperinsulinaemia and high levels of luteinizing hormone are seen in PCOS and there appears to be some overlap with the metabolic syndrome.

#### General

- weight reduction if appropriate
- if a women requires contraception then a combined oral contraceptive (COC) pill may help regulate her cycle and induce a monthly bleed (see below)

#### Hirsutism and acne

- a COC pill may be used help manage hirsutism. Possible options include a third generation COC which has fewer androgenic effects or co-cyprindiol which has an anti-androgen action. Both of these types of COC may carry an increased risk of venous thromboembolism
- if doesn't respond to COC then topical eflornithine may be tried
- spironolactone, flutamide and finasteride may be used under specialist supervision

#### Infertility

- weight reduction if appropriate
- the management of infertility in patients with PCOS should be supervised by a specialist. There is an ongoing debate as to whether metformin, clomifene or a combination should be used to stimulate ovulation

- a 2007 trial published in the New England Journal of Medicine suggested clomifene was the most effective treatment. There is a potential risk of multiple pregnancies with anti-oestrogen\* therapies such as clomifene. The RCOG published an opinion paper in 2008 and concluded that on current evidence metformin is

not a first line treatment of choice in the management of PCOS

- metformin is also used, either combined with clomifene or alone, particularly in patients who are obese
- gonadotrophins

\*work by occupying hypothalamic oestrogen receptors without activating them. This interferes with the binding of oestradiol and thus prevents negative feedback inhibition of FSH secretion

A 69-year-old woman with a history of learning difficulties is reviewed in clinic. She is known to have erythema ab igne on her legs but according to her carer still spends long hours in front of her electric fire. Which one of the following skin lesions is she at risk of developing?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Squamous cell carcinoma               |
| <input type="radio"/> | B. Cutaneous T-cell lymphoma of the skin |
| <input type="radio"/> | C. Dermatofibrosarcoma protuberans       |
| <input type="radio"/> | D. Basal cell carcinoma                  |
| <input type="radio"/> | E. Malignant melanoma                    |

[Next question](#)

### Erythema ab igne

Erythema ab igne is a skin disorder caused by over exposure to infrared radiation. Characteristic features include reticulated, erythematous patches with hyperpigmentation and telangiectasia. A typical history would be an elderly women who always sits next to an open fire

If the cause is not treated then patients may go on to develop squamous cell skin cancer

**Question 105 of 129**

Next

A 43-year-old woman who is a recent immigrant from Mozambique is referred to the dermatology outpatient clinic. She has developed a number of hypopigmented, oval shaped lesions on her body which are associated with reduced sensation. These are mainly located on the extensor surfaces of her limbs. She has no past medical history of note other than suffering from malaria as a child. What is the most likely diagnosis?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. HIV                   |
| <input type="radio"/> | B. Chagas disease        |
| <input type="radio"/> | C. Pityriasis versicolor |
| <input type="radio"/> | D. Tuberculosis          |
| <input type="radio"/> | E. Leprosy               |

Next question

**Leprosy**

Leprosy is a granulomatous disease primarily affecting the peripheral nerves and skin. It is caused by *Mycobacterium leprae*.

**Features**

- patches of hypopigmented skin typically affecting the buttocks, face, and extensor surfaces of limbs
- sensory loss

The degree of cell mediated immunity determines the type of leprosy a patient will develop.

Low degree of cell mediated immunity --> lepromatous leprosy ('multibacillary')

- extensive skin involvement
- symmetrical nerve involvement

High degree of cell mediated immunity --> tuberculoid leprosy ('paucibacillary')

- limited skin disease
- asymmetric nerve involvement

**Management**

- WHO-recommended triple therapy: rifampicin, dapsone and clofazimine

Which one of the following is least recognised as a cause of erythroderma in the UK?

<input type="radio"/>	A. Lymphoma
<input type="radio"/>	B. Drug eruption
<input type="radio"/>	C. Lichen planus
<input type="radio"/>	D. Psoriasis
<input type="radio"/>	E. Eczema

Next question

## Erythroderma

Erythroderma is a term used when more than 95% of the skin is involved in a rash of any kind

Causes of erythroderma

- eczema
- psoriasis
- drugs e.g. gold
- lymphoma, leukaemia
- idiopathic

Erythrodermic psoriasis

- may result from progression of chronic disease to an exfoliative phase with plaques covering most of the body. Associated with mild systemic upset
- more serious form is an acute deterioration. This may be triggered by a variety of factors such as withdrawal of systemic steroids. Patients need to be admitted to hospital for management

A patient develops an eczematous, weeping rash on his wrist following the purchase of a new watch. In the Gell and Coombs classification of hypersensitivity reactions this is an example of a:

<input type="radio"/>	A. Type I reaction
<input type="radio"/>	B. Type II reaction
<input type="radio"/>	C. Type III reaction
<input type="radio"/>	D. Type IV reaction
<input type="radio"/>	E. Type V reaction

[Next question](#)

This patient has allergic contact dermatitis, which is commonly precipitated by nickel

### Hypersensitivity

The Gell and Coombs classification divides hypersensitivity reactions into 4 types

#### Type I - Anaphylactic

- antigen reacts with IgE bound to mast cells
- anaphylaxis, atopy

#### Type II - Cell bound

- IgG or IgM binds to antigen on cell surface
- autoimmune haemolytic anaemia, ITP, Goodpasture's

#### Type III - Immune complex

- free antigen and antibody (IgG, IgA) combine
- serum sickness, systemic lupus erythematosus, post-streptococcal glomerulonephritis, extrinsic allergic alveolitis (especially acute phase)

#### Type IV - Delayed hypersensitivity

- T cell mediated
- tuberculosis, tuberculin skin reaction, graft versus host disease, allergic contact dermatitis, scabies, extrinsic allergic alveolitis (especially chronic phase)

In recent times a further category has been added:

## Type V - Stimulated hypersensitivity

- IgG antibodies stimulate cells they are directed against
- Graves', myasthenia gravis



A 72-year-old woman who is known to have type 2 diabetes mellitus and heart failure is reviewed. One week ago she was treated with oral flucloxacillin and penicillin V for a right lower limb cellulitis. Unfortunately there has been no response to treatment. What is the most appropriate next line antibiotic?

- |                       |                 |
|-----------------------|-----------------|
| <input type="radio"/> | A. Co-amoxiclav |
| <input type="radio"/> | B. Erythromycin |
| <input type="radio"/> | C. Clindamycin  |
| <input type="radio"/> | D. Vancomycin   |
| <input type="radio"/> | E. Gentamicin   |

[Next question](#)

### Cellulitis: management

The BNF recommends flucloxacillin as first-line treatment for mild/moderate cellulitis. Clarithromycin or clindamycin is recommended in patients allergic to penicillin.

Many local protocols now suggest the use of oral clindamycin in patients who have failed to respond to flucloxacillin.

Severe cellulitis should be treated with intravenous benzylpenicillin + flucloxacillin.

A 14-year-old male is reviewed due to a patch of scaling and hair loss on the right side of his head. A skin scraping is sent which confirms a diagnosis of tinea capitis. Which organism is most likely to be responsible?

<input type="radio"/>	A. <i>Trichophyton tonsurans</i>
<input type="radio"/>	B. <i>Microsporum distortum</i>
<input type="radio"/>	C. <i>Trichophyton verrucosum</i>
<input type="radio"/>	D. <i>Microsporum audouinii</i>
<input type="radio"/>	E. <i>Microsporum canis</i>

[Next question](#)

## Tinea

Tinea is a term given to dermatophyte fungal infections. Three main types of infection are described depending on what part of the body is infected

- tinea capitis - scalp
- tinea corporis - trunk, legs or arms
- tinea pedis - feet

### Tinea capitis (scalp ringworm)

- a cause of scarring alopecia mainly seen in children
- if untreated a raised, pustular, spongy/boggy mass called a kerion may form
- most common cause is *Trichophyton tonsurans* in the UK and the USA
- may also be caused by *Microsporum canis* acquired from cats or dogs
- diagnosis: lesions due to *Microsporum canis* green fluorescence under Wood's lamp\*. However the most useful investigation is scalp scrapings
- management (based on CKS guidelines): oral antifungals: terbinafine for *Trichophyton tonsurans* infections and griseofulvin for *Microsporum* infections. Topical ketoconazole shampoo should be given for the first two weeks to reduce transmission

### Tinea corporis

- causes include *Trichophyton rubrum* and *Trichophyton verrucosum* (e.g. From contact with cattle)
- well-defined annular, erythematous lesions with pustules and papules
- may be treated with oral fluconazole

### Tinea pedis (athlete's foot)

- characterised by itchy, peeling skin between the toes
- common in adolescence

\*lesions due to Trichophyton species do not readily fluoresce under Wood's lamp

A 67-year-old man with recurrent actinic keratoses on his scalp is reviewed. Which one of the following is not a treatment option for the management of this condition?

<input type="radio"/>	A. Topical diclofenac
<input type="radio"/>	B. Topical betnovate
<input type="radio"/>	C. Topical fluorouracil
<input type="radio"/>	D. Topical imiquimod
<input type="radio"/>	E. Cryotherapy

[Next question](#)

### Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

#### Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

#### Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

A 72-year-old man is investigated for oral ulceration. A biopsy suggests pemphigus vulgaris. This is most likely to be caused by antibodies directed against:

<input type="radio"/>	A. Hemidesmosomal BP180
<input type="radio"/>	B. Occludin-2
<input type="radio"/>	C. Hemidesmosomal BP230
<input type="radio"/>	D. Desmoglein
<input type="radio"/>	E. Adherens

[Next question](#)

### Pemphigus vulgaris

Pemphigus vulgaris is an autoimmune disease caused by antibodies directed against desmoglein, a cadherin-type epithelial cell adhesion molecule. It is more common in the Ashkenazi Jewish population

#### Features

- mucosal ulceration is common and often the presenting symptom. Oral involvement is seen in 50-70% of patients
- skin blistering - flaccid, easily ruptured vesicles and bullae. Lesions are typically painful but not itchy. These may develop months after the initial mucosal symptoms. Nikolsky's describes the spread of bullae following application of horizontal, tangential pressure to the skin
- acantholysis on biopsy

#### Management

- steroids
- immunosuppressants

Which one of the following drugs is most likely to result in a photosensitive rash?

<input type="radio"/>	A. Gentamicin
<input type="radio"/>	B. Erythromycin
<input type="radio"/>	C. Penicillin
<input type="radio"/>	D. Tetracycline
<input type="radio"/>	E. Amoxicillin

Next question

### Drugs causing photosensitivity

Causes of drug-induced photosensitivity

- thiazides
- tetracyclines, sulphonamides, ciprofloxacin
- amiodarone
- NSAIDs e.g. piroxicam
- psoralens
- sulphonylureas

**Question 113 of 129**

Next

A 78-year-old woman asks you for cream to treat a lesion on her left cheek. It has been present for the past nine months and is asymptomatic. On examination you find a 2 \* 3 cm area of flat brown pigmentation with a jagged, irregular edge. The pigmentation on the anterior aspect of the lesion is a darker brown. What is the most likely diagnosis?

- |                       |                          |
|-----------------------|--------------------------|
| <input type="radio"/> | A. Solar lentigo         |
| <input type="radio"/> | B. Dermatofibroma        |
| <input type="radio"/> | C. Lentigo maligna       |
| <input type="radio"/> | D. Bowen's disease       |
| <input type="radio"/> | E. Seborrhoeic keratosis |

Next question

These lesions often present a diagnostic dilemma. The asymmetrical nature of the lesion would however point away from a diagnosis of solar lentigo.

**Lentigo maligna**

Lentigo maligna is a type of melanoma in-situ. It typically progresses slowly but may at some stage become invasive causing lentigo maligna melanoma.

A 45-year-old man who presented with itchy lesions on his hands is diagnosed with scabies. It is decided to treat him with permethrin 5%. You have explained the need to treat all members of the household and hot wash all bedding and clothes. What advice should be given about applying the cream?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. From neck down + leave for 12 hours                               |
| <input type="radio"/> | B. All skin including scalp + leave for 12 hours + retreat in 2 days |
| <input type="radio"/> | C. All skin including scalp + leave for 12 hours + retreat in 7 days |
| <input type="radio"/> | D. From neck down + leave for 4 hours                                |
| <input type="radio"/> | E. From neck down + leave for 12 hours + retreat in 7 days           |

[Next question](#)

Scabies - permethrin treatment: all skin including scalp + leave for 12 hours + retreat in 7 days

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation (and common practice).

## Scabies

Scabies is caused by the mite *Sarcoptes scabiei* and is spread by prolonged skin contact. It typically affects children and young adults.

The scabies mite burrows into the skin, laying its eggs in the stratum corneum. The intense pruritus associated with scabies is due to a delayed type IV hypersensitivity reaction to mites/eggs which occurs about 30 days after the initial infection.

### Features

- widespread pruritus
- linear burrows on the side of fingers, interdigital webs and flexor aspects of the wrist
- in infants the face and scalp may also be affected
- secondary features are seen due to scratching: excoriation, infection

### Management

- permethrin 5% is first-line
- malathion 0.5% is second-line
- give appropriate guidance on use (see below)
- pruritus persists for up to 4-6 weeks post eradication



## Patient guidance on treatment (from Clinical Knowledge Summaries)

- avoid close physical contact with others until treatment is complete
- all household and close physical contacts should be treated at the same time, even if asymptomatic
- launder, iron or tumble dry clothing, bedding, towels, etc., on the first day of treatment to kill off mites.

The BNF advises to apply the insecticide to all areas, including the face and scalp, contrary to the manufacturer's recommendation. Patients should be given the following instructions:

- apply the insecticide cream or liquid to cool, dry skin
- pay close attention to areas between fingers and toes, under nails, armpit area, creases of the skin such as at the wrist and elbow
- allow to dry and leave on the skin for 8-12 hours for permethrin, or for 24 hours for malathion, before washing off
- reapply if insecticide is removed during the treatment period, e.g. If wash hands, change nappy, etc
- repeat treatment 7 days later

A 17-year-old male is reviewed six weeks after starting an oral antibiotic for acne vulgaris. He stopped taking the drug two weeks ago due to perceived alteration in his skin colour, and denies been exposed to strong sunlight for the past six months. On examination he has generalised increased skin pigmentation, including around the buttocks. Which one of the following antibiotics was he likely to be taking?

- |                       |                    |
|-----------------------|--------------------|
| <input type="radio"/> | A. Doxycycline     |
| <input type="radio"/> | B. Oxytetracycline |
| <input type="radio"/> | C. Tetracycline    |
| <input type="radio"/> | D. Erythromycin    |
| <input type="radio"/> | E. Minocycline     |

[Next question](#)

Minocycline can cause irreversible skin pigmentation and is now considered a second line drug in acne. Photosensitivity secondary to tetracycline/doxycycline is less likely given the generalised distribution of the pigmentation and the failure to improve following drug withdrawal

### Acne vulgaris: management

Acne vulgaris is a common skin disorder which usually occurs in adolescence. It typically affects the face, neck and upper trunk and is characterised by the obstruction of the pilosebaceous follicles with keratin plugs which results in comedones, inflammation and pustules.

Acne may be classified into mild, moderate or severe:

- mild: open and closed comedones with or without sparse inflammatory lesions
- moderate acne: widespread non-inflammatory lesions and numerous papules and pustules
- severe acne: extensive inflammatory lesions, which may include nodules, pitting, and scarring

A simple step-up management scheme often used in the treatment of acne is as follows:

- single topical therapy (topical retinoids, benzyl peroxide)
- topical combination therapy (topical antibiotic, benzoyl peroxide, topical retinoid)
- oral antibiotics: e.g. Oxytetracycline, doxycycline. Improvement may not be seen for 3-4 months. Minocycline is now considered less appropriate due to the possibility of irreversible pigmentation. Gram negative folliculitis may occur as a complication of long-term antibiotic use - high-dose oral trimethoprim is effective if this occurs
- oral isotretinoin: only under specialist supervision

There is no role for dietary modification in patients with acne

A 67-year-old man is diagnosed with actinic keratoses on his right temple and prescribed fluorouracil cream. One week later he presents as the skin where he is applying treatment has become red and sore. On examination there is no sign of weeping or blistering. What is the most appropriate action?

<input type="radio"/>	A. Continue fluorouracil cream + review in 1 week
<input type="radio"/>	B. Complete a 'Yellow Card'
<input type="radio"/>	C. Stop fluorouracil cream + prescribe topical hydrocortisone
<input type="radio"/>	D. Continue fluorouracil cream + prescribe topical hydrocortisone to use concurrently
<input type="radio"/>	E. Stop fluorouracil cream

[Next question](#)

This is a normal reaction to treatment. Fluorouracil should be continued for at least another week before starting topical steroids.

### Actinic keratoses

Actinic, or solar, keratoses (AK) is a common premalignant skin lesion that develops as a consequence of chronic sun exposure

#### Features

- small, crusty or scaly, lesions
- may be pink, red, brown or the same colour as the skin
- typically on sun-exposed areas e.g. temples of head
- multiple lesions may be present

#### Management options include

- prevention of further risk: e.g. sun avoidance, sun cream
- fluorouracil cream: typically a 2 to 3 week course. The skin will become red and inflamed - sometimes topical hydrocortisone is given following fluorouracil to help settle the inflammation
- topical diclofenac: may be used for mild AKs. Moderate efficacy but much fewer side-effects
- topical imiquimod: trials have shown good efficacy
- cryotherapy
- curettage and cautery

A 19-year-old man is started on isotretinoin for severe nodulo-cystic acne. Which one of the following side-effects is most likely to occur?

<input type="radio"/>	A. Low mood
<input type="radio"/>	B. Thrombocytopaenia
<input type="radio"/>	C. Raised plasma triglycerides
<input type="radio"/>	D. Reversible alopecia
<input type="radio"/>	E. Dry skin

[Next question](#)

Dry skin is the most common side-effect of isotretinoin

### Isotretinoin

Isotretinoin is an oral retinoid used in the treatment of severe acne. Two-thirds of patients have a long term remission or cure following a course of oral isotretinoin

#### Adverse effects

- teratogenicity: females should ideally be using two forms of contraception (e.g. Combined oral contraceptive pill and condoms)
- dry skin, eyes and lips: the most common side-effect of isotretinoin
- low mood
- raised triglycerides
- hair thinning
- nose bleeds (caused by dryness of the nasal mucosa)
- benign intracranial hypertension: isotretinoin treatment should not be combined with tetracyclines for this reason

Which one of the following statements regarding fungal nail infections is incorrect?

<input type="radio"/>	A. <i>Candida</i> accounts for less than 10% of cases
<input type="radio"/>	B. Diagnosis should be confirmed by microbiology before starting treatment
<input type="radio"/>	C. Treatment is successful in around 90-95% of people
<input type="radio"/>	D. Thickened, rough, opaque nails are typical
<input type="radio"/>	E. Suitable investigations include nail clippings

Next question

## Fungal nail infections

Onychomycosis is fungal infection of the nails. This may be caused by

- dermatophytes - mainly *Trichophyton rubrum*, accounts for 90% of cases
- yeasts - such as *Candida*
- non-dermatophyte moulds

### Features

- 'unsightly' nails are a common reason for presentation
- thickened, rough, opaque nails are the most common finding

### Investigation

- nail clippings
- scrapings of the affected nail

### Management

- treatment is successful in around 50-80% of people
- diagnosis should be confirmed by microbiology before starting treatment
- dermatophyte infection: oral terbinafine is currently recommended first-line with oral itraconazole as an alternative. Six weeks - 3 months therapy is needed for fingernail infections whilst toenails should be treated for 3 - 6 months
- *Candida* infection: mild disease should be treated with topical antifungals (e.g. Amorolfine) whilst more severe infections should be treated with oral itraconazole for a period of 12 weeks

A 65-year-old woman with blistering lesions on her leg is diagnosed as having bullous pemphigoid. What is the most appropriate initial management?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Reassurance                          |
| <input type="radio"/> | B. Topical corticosteroids              |
| <input type="radio"/> | C. Oral itraconazole                    |
| <input type="radio"/> | D. Screen for solid-tumour malignancies |
| <input type="radio"/> | E. Oral corticosteroids                 |

Next question

### Bullous pemphigoid

Bullous pemphigoid is an autoimmune condition causing sub-epidermal blistering of the skin. This is secondary to the development of antibodies against hemidesmosomal proteins BP180 and BP230

Bullous pemphigoid is more common in elderly patients. Features include

- itchy, tense blisters typically around flexures
- the blisters usually heal without scarring
- mouth is usually spared\*

Skin biopsy

- immunofluorescence shows IgG and C3 at the dermoepidermal junction

Management

- referral to dermatologist for biopsy and confirmation of diagnosis
- oral corticosteroids are the mainstay of treatment
- topical corticosteroids, immunosuppressants and antibiotics are also used

\*in reality around 10-50% of patients have a degree of mucosal involvement. It would however be unusual for an exam question to mention mucosal involvement as it is seen as a classic differentiating feature between pemphigoid and pemphigus.

Each one of the following is associated with hypertrichosis, except:

<input type="radio"/>	A. Anorexia nervosa
<input type="radio"/>	B. Porphyria cutanea tarda
<input type="radio"/>	C. Psoriasis
<input type="radio"/>	D. Minoxidil
<input type="radio"/>	E. Ciclosporin

Next question

### Hirsutism and hypertrichosis

/hirsutism is often used to describe androgen-dependent hair growth in women, with hypertrichosis being used for androgen-independent hair growth

Polycystic ovarian syndrome is the most common causes of hirsutism. Other causes include:

- Cushing's syndrome
- congenital adrenal hyperplasia
- androgen therapy
- obesity: due to peripheral conversion oestrogens to androgens
- adrenal tumour
- androgen secreting ovarian tumour
- drugs: phenytoin

#### Assessment of hirsutism

- Ferriman-Gallwey scoring system: 9 body areas are assigned a score of 0 - 4, a score > 15 is considered to indicate moderate or severe hirsutism

#### Management of hirsutism

- advise weight loss if overweight
- cosmetic techniques such as waxing/bleaching - not available on the NHS
- consider using combined oral contraceptive pills such as co-cyprindiol (Dianette) or ethinylestradiol and drospirenone (Yasmin). Co-cyprindiol should not be used long-term due to the increased risk of venous thromboembolism
- facial hirsutism: topical eflornithine - contraindicated in pregnancy and breast-feeding

## Causes of hypertrichosis

- drugs: minoxidil, ciclosporin, diazoxide
- congenital hypertrichosis lanuginosa, congenital hypertrichosis terminalis
- porphyria cutanea tarda
- anorexia nervosa



Which one of the following antibiotics is most associated with the development of Stevens-Johnson syndrome?

<input type="radio"/>	A. Co-trimoxazole
<input type="radio"/>	B. Ethambutol
<input type="radio"/>	C. Chloramphenicol
<input type="radio"/>	D. Ciprofloxacin
<input type="radio"/>	E. Gentamicin

Next question

### Stevens-Johnson syndrome

Stevens-Johnson syndrome severe form of erythema multiforme associated with mucosal involvement and systemic symptoms

#### Features

- rash is typically maculopapular with target lesions being characteristic. May develop into vesicles or bullae
- mucosal involvement
- systemic symptoms: fever, arthralgia

#### Causes

- idiopathic
- bacteria: Mycoplasma, *Streptococcus*
- viruses: herpes simplex virus, Orf
- drugs: penicillin, sulphonamides, carbamazepine, allopurinol, NSAIDs, oral contraceptive pill
- connective tissue disease e.g. SLE
- sarcoidosis
- malignancy

A 33-year-old man presents complaining of an itchy scalp and dandruff. On examination he is noted to have eczema on his scalp, behind his ears and around his nose. He has tried 'Head and Shoulders' and 'Neutrogen T-gel' but with poor results. Which one of the following is the most appropriate treatment for his scalp?

<input type="radio"/>	A. Topical hydrocortisone
<input type="radio"/>	B. Oral metronidazole
<input type="radio"/>	C. Topical selenium sulphide
<input type="radio"/>	D. Oral terbinafine
<input type="radio"/>	E. Topical ketoconazole

[Next question](#)

### Seborrhoeic dermatitis in adults

Seborrhoeic dermatitis in adults is a chronic dermatitis thought to be caused by an inflammatory reaction related to a proliferation of a normal skin inhabitant, a fungus called *Malassezia furfur* (formerly known as *Pityrosporum ovale*). It is common, affecting around 2% of the general population

#### Features

- eczematous lesions on the sebum-rich areas: scalp (may cause dandruff), periorbital, auricular and nasolabial folds
- otitis externa and blepharitis may develop

#### Associated conditions include

- HIV
- Parkinson's disease

#### Scalp disease management

- over the counter preparations containing zinc pyrithione ('Head & Shoulders') and tar ('Neutrogena T/Gel') are first-line
- the preferred second-line agent is ketoconazole
- selenium sulphide and topical corticosteroid may also be useful

#### Face and body management

- topical antifungals: e.g. Ketoconazole
- topical steroids: best used for short periods
- difficult to treat - recurrences are common

A 34-year-old patient who is known to have psoriasis presents with erythematous skin in the groin and genital area. He also has erythematous skin in the axilla. In the past he has expressed a dislike of messy or cumbersome creams. What is the most appropriate treatment?

- |                       |                         |
|-----------------------|-------------------------|
| <input type="radio"/> | A. Topical steroid      |
| <input type="radio"/> | B. Topical dithranol    |
| <input type="radio"/> | C. Topical clotrimazole |
| <input type="radio"/> | D. Coal tar             |
| <input type="radio"/> | E. Topical calcipotriol |

Next question

Flexural psoriasis - topical steroid

This patient has flexural psoriasis which responds well to topical steroids. Topical calcipotriol is usually irritant in flexures. Mild tar preparations are an option but may be messy and cumbersome.

### Psoriasis: management

SIGN released guidelines in 2010 on the management of psoriasis and psoriatic arthropathy. Please see the link for more details.

#### Chronic plaque psoriasis

- regular emollients may help to reduce scale loss and reduce pruritus
- for acute control SIGN recommend: 'Short term intermittent use of a potent topical corticosteroid or a combined potent corticosteroid plus calcipotriol

ointment is recommended to gain rapid improvement in plaque psoriasis.'

- 'For long term topical treatment of plaque psoriasis a vitamin D analogue (e.g. Calcipotriol) is recommended.'
- 'If a vitamin D analogue is ineffective or not tolerated then consider coal tar (solution, cream or lotion), tazarotene gel, or short contact dithranol (30 minute exposure in patients with a small number of relatively large plaques of psoriasis).

#### Steroids in psoriasis

- topical steroids are commonly used in flexural psoriasis and there is also a role for mild steroids in facial psoriasis. If steroids are ineffective for these conditions vitamin D analogues or tacrolimus ointment should be used second line

- SIGN caution against the long term use of potent or very potent topical steroids due to the risk of side-effects

### Scalp psoriasis

- for short term control SIGN recommend either the use of potent topical corticosteroids or a combination of a potent corticosteroid and a vitamin D

### analogue

- 'For patients with thick scaling of the scalp, initial treatment with overnight application of salicylic acid, tar preparations, or oil preparations (eg olive oil, coconut oil) to remove thick scale is recommended.

## Secondary care management

### Phototherapy

- narrow band ultraviolet B light (311-313nm) is now the treatment of choice
- photochemotherapy is also used - psoralen + ultraviolet A light (PUVA)
- adverse effects: skin ageing, squamous cell cancer (not melanoma)

### Systemic therapy

- methotrexate: useful if associated joint disease
- ciclosporin
- systemic retinoids
- biological agents: infliximab, etanercept and adalimumab
- ustekinumab (IL-12 and IL-23 blocker) is showing promise in early trials

### Mechanism of action of commonly used drugs:

- coal tar: probably inhibit DNA synthesis
- calcipotriol: vitamin D analogue which reduces epidermal proliferation and restores a normal horny layer
- dithranol: inhibits DNA synthesis, wash off after 30 mins, SE: burning, staining

Which one of the following statements regarding vitiligo is true?

<input type="radio"/>	A. It is seen in around 0.1% of patients
<input type="radio"/>	B. The average age of onset is 40-50 years
<input type="radio"/>	C. Skin trauma may precipitate new skin lesions
<input type="radio"/>	D. It is rare in Caucasian people
<input type="radio"/>	E. The torso tends to be affected first

Next question

This is known as the Koebner phenomenon

### Vitiligo

Vitiligo is an autoimmune condition which results in the loss of melanocytes and consequent depigmentation of the skin. It is thought to affect around 1% of the population and symptoms typically develop by the age of 20-30 years.

#### Features

- well demarcated patches of depigmented skin
- the peripheries tend to be most affected
- trauma may precipitate new lesions (Koebner phenomenon)

#### Associated conditions

- type 1 diabetes mellitus
- Addison's disease
- autoimmune thyroid disorders
- pernicious anaemia
- alopecia areata

#### Management

- sun block for affected areas of skin
- camouflage make-up
- topical corticosteroids may reverse the changes if applied early
- there may also be a role for topical tacrolimus and phototherapy, although caution needs to be exercised with light-skinned patients

**Question 125 of 129**

Next

A 50-year-old man presents with shiny, flat-topped papules on the palmar aspect of the wrists. He is mainly bothered by the troublesome and persistent itching. A diagnosis of lichen planus is suspected. What is the most appropriate treatment?

<input type="radio"/>	A. Refer for punch biopsy
<input type="radio"/>	B. Emollients + oral antihistamine
<input type="radio"/>	C. Topical dapsone
<input type="radio"/>	D. Topical clotrimazole
<input type="radio"/>	E. Topical clobetasone butyrate

Next question

**Lichen planus**

Lichen planus is a skin disorder of unknown aetiology, most probably being immune mediated

**Features**

- itchy, papular rash most common on the palms, soles, genitalia and flexor surfaces of arms
- rash often polygonal in shape, 'white-lace' pattern on the surface (Wickham's striae)
- Koebner phenomenon may be seen (new skin lesions appearing at the site of trauma)
- oral involvement in around 50% of patients
- nails: thinning of nail plate, longitudinal ridging

Lichenoid drug eruptions - causes:

- gold
- quinine
- thiazides

**Management**

- topical steroids are the mainstay of treatment
- extensive lichen planus may require oral steroids or immunosuppression

Which of the following skin conditions associated with malignancy are not correctly paired?

- ☐ A. Erythroderma and lymphoma
- ☐ B. Necrolytic migratory erythema and gastrinoma
- ☐ C. Acanthosis nigricans and gastrointestinal cancer
- ☐ D. Sweet's syndrome and myelodysplasia
- ☐ E. Erythema gyratum repens and lung cancer

Next question

Necrolytic migratory erythema is associated with glucagonomas

### Skin disorders associated with malignancy

Paraneoplastic syndromes associated with internal malignancies:

Skin disorder	Associated malignancies
Acanthosis nigricans	Gastric cancer
Acquired ichthyosis	Lymphoma
Acquired hypertrichosis lanuginosa	Gastrointestinal and lung cancer
Dermatomyositis	Ovarian and lung cancer
Erythema gyratum repens	Lung cancer
Erythroderma	Lymphoma
Migratory thrombophlebitis	Pancreatic cancer
Necrolytic migratory erythema	Glucagonoma
Pyoderma gangrenosum (bullous and non-bullous forms)	Myeloproliferative disorders
Sweet's syndrome	Haematological malignancy e.g. Myelodysplasia - tender, purple plaques
Tylosis	Oesophageal cancer

A 30-year-old man presents with painful, purple coloured lesions on his shins. Some of these lesions have started to heal and no evidence of scarring is seen. These have been present for the past 2 weeks. There is no past medical history of note and he takes no regular medications. What is the most useful next investigation?

<input type="radio"/>	A. Liver function tests
<input type="radio"/>	B. Anti-nuclear antibody
<input type="radio"/>	C. ECG
<input type="radio"/>	D. HIV test
<input type="radio"/>	E. Chest x-ray

[Next question](#)

The likely diagnosis here is erythema nodosum (EN). All these tests may have a place but a chest x-ray is important as it helps exclude sarcoidosis and tuberculosis, two important cause of EN

## Erythema nodosum

### Overview

- inflammation of subcutaneous fat
- typically causes tender, erythematous, nodular lesions
- usually occurs over shins, may also occur elsewhere (e.g. forearms, thighs)
- usually resolves within 6 weeks
- lesions heal without scarring

### Causes

- infection: streptococci, TB, brucellosis
- systemic disease: sarcoidosis, inflammatory bowel disease, Behcet's
- malignancy/lymphoma
- drugs: penicillins, sulphonamides, combined oral contraceptive pill
- pregnancy



A 36-year-old female with a history of ulcerative colitis is diagnosed as having pyoderma gangrenosum. She presented 4 days ago with a 1 cm lesion on her right shin which rapidly ulcerated and is now painful. What is the most appropriate management?

<input type="radio"/>	A. Topical hydrocortisone
<input type="radio"/>	B. Oral prednisolone
<input type="radio"/>	C. Surgical debridement
<input type="radio"/>	D. Topical tacrolimus
<input type="radio"/>	E. Infliximab

[Next question](#)

Topical therapy does have a role in pyoderma gangrenosum and it may seem intuitive to try this first before moving on to systemic treatment. However, pyoderma gangrenosum has the potential to evolve rapidly and for this reason oral prednisolone is usually given as initial treatment. For a review see BMJ 2006;333:181-184

### Pyoderma gangrenosum

#### Features

- typically on the lower limbs
- initially small red papule
- later deep, red, necrotic ulcers with a violaceous border
- may be accompanied systemic symptoms e.g. Fever, myalgia

#### Causes\*

- idiopathic in 50%
- inflammatory bowel disease: ulcerative colitis, Crohn's
- rheumatoid arthritis, SLE
- myeloproliferative disorders
- lymphoma, myeloid leukaemias
- monoclonal gammopathy (IgA)
- primary biliary cirrhosis

#### Management

- the potential for rapid progression is high in most patients and most doctors advocate oral steroids as first-line treatment
- other immunosuppressive therapy, for example ciclosporin and infliximab, have a role in difficult cases

\*note whilst pyoderma gangrenosum can occur in diabetes mellitus it is rare and is generally not included in a differential of potential causes

### Question 129 of 129

A man presents with an area of dermatitis on his left wrist. He thinks he may be allergic to nickel. Which one of the following is the best test to investigate this possibility?

- ☐ A. Skin patch test
- ☐ B. Radioallergosorbent test (RAST)
- ☐ C. Nickel IgG levels
- ☐ D. Skin prick test
- ☐ E. Nickel IgM levels

### Allergy tests

<b>Skin prick test</b>	<p>Most commonly used test as easy to perform and inexpensive. Drops of diluted allergen are placed on the skin after which the skin is pierced using a needle. A large number of allergens can be tested in one session. Normally includes a histamine (positive) and sterile water (negative) control. A wheal will typically develop if a patient has an allergy. Can be interpreted after 15 minutes</p> <p>Useful for food allergies and also pollen</p>
<b>Radioallergosorbent test (RAST)</b>	<p>Determines the amount of IgE that reacts specifically with suspected or known allergens, for example IgE to egg protein. Results are given in grades from 0 (negative) to 6 (strongly positive)</p> <p>Useful for food allergies, inhaled allergens (e.g. Pollen) and wasp/bee venom</p> <p>Blood tests may be used when skin prick tests are not suitable, for example if there is extensive eczema or if the patient is taking antihistamines</p>
<b>Skin patch testing</b>	<p>Useful for contact dermatitis. Around 30-40 allergens are placed on the back. Irritants may also be tested for. The patches are removed 48 hours later with the results being read by a dermatologist after a further 48 hours</p>

### Question 1 of 54

Next

A 65-year-old man with a 16 year history of type 2 diabetes mellitus presents complaining of poor eye sight and blurred vision. Visual acuity measured using a Snellen chart is reduced to 6/12 in the right eye and 6/18 in the left eye. Fundoscopy reveals a number of yellow deposits in the left eye consistent with drusen formation. Similar changes but to a lesser extent are seen in the right eye. What is the most likely diagnosis?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Wet age-related macular degeneration   |
| <input type="radio"/> | B. Pre-proliferative diabetic retinopathy |
| <input type="radio"/> | C. Chronic open angle glaucoma            |
| <input type="radio"/> | D. Proliferative diabetic retinopathy     |
| <input type="radio"/> | E. Dry age-related macular degeneration   |

Next question

**Drusen = Dry macular degeneration**

### Age related macular degeneration

Age related macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral.

Traditionally two forms of macular degeneration are seen:

- dry (geographic atrophy) macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis

Recently there has been a move to a more updated classification:

- early age related macular degeneration (non-exudative, age related maculopathy): drusen and alterations to the retinal pigment epithelium (RPE)
- late age related macular degeneration (neovascularisation, exudative)

Risk factors

- age: most patients are over 60 years of age
- smoking

- family history
- more common in Caucasians
- high cumulative sunlight exposure
- female sex

## Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

## Investigation and diagnosis

- optical coherence tomography: provide cross sectional views of the macula
- if neovascularisation is present fluorescein angiography is performed

## General management

- stop smoking
- high dose of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Supplements should be avoided in smokers due to an increased risk of lung cancer

## Dry macular degeneration - no current medical treatments

## Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

## Question 2 of 54

Next

Which one of the following is associated with the Holmes-Adie pupil?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Decreased ankle reflexes                      |
| <input type="radio"/> | B. Pupillary constriction                        |
| <input type="radio"/> | C. Ptosis in 10-20% of cases                     |
| <input type="radio"/> | D. An increased of developing multiple sclerosis |
| <input type="radio"/> | E. Neurosyphilis                                 |

Next question

Holmes ADie = DIlated pupil, females, absent leg reflexes

### Holmes-Adie pupil

Holmes-Adie pupil is a benign condition most commonly seen in women. It is one of the differentials of a dilated pupil.

#### Overview

- unilateral in 80% of cases
- dilated pupil
- once the pupil has constricted it remains small for an abnormally long time
- slowly reactive to accommodation but very poorly (if at all) to light

#### Holmes-Adie syndrome

- association of Holmes-Adie pupil with absent ankle/knee reflexes

A 71-year-old man presents with a burning sensation around his right eye. On examination an erythematous blistering rash can be seen in the right trigeminal distribution. What is the most likely diagnosis?

<input type="radio"/>	A. Ramsay Hunt syndrome
<input type="radio"/>	B. Cluster headache
<input type="radio"/>	C. Fungal keratitis
<input type="radio"/>	D. Herpes zoster ophthalmicus
<input type="radio"/>	E. Trigeminal neuralgia

[Next question](#)

### Herpes zoster ophthalmicus

Herpes zoster ophthalmicus (HZO) describes the reactivation of the varicella zoster virus in the area supplied by the ophthalmic division of the trigeminal nerve. It accounts for around 10% of cases of shingles.

#### Features

- vesicular rash around the eye, which may or may not involve the actual eye itself
- Hutchinson's sign: rash on the tip or side of the nose. Indicates nasociliary involvement and is a strong risk factor for ocular involvement

#### Management

- oral antiviral treatment for 7-10 days, ideally started within 72 hours. Topical antiviral treatment is not given in HZO
- oral corticosteroids may reduce the duration of pain but do not reduce the incidence of post-herpetic neuralgia
- ocular involvement requires urgent ophthalmology review

#### Complications

- ocular: conjunctivitis, keratitis, episcleritis, anterior uveitis
- ptosis
- post-herpetic neuralgia

Which one of the following is least associated with the development of optic atrophy?

<input type="radio"/>	A. Ataxic telangiectasia
<input type="radio"/>	B. Longstanding papilloedema
<input type="radio"/>	C. Multiple sclerosis
<input type="radio"/>	D. Glaucoma
<input type="radio"/>	E. Retinitis pigmentosa

Next question

### Optic atrophy

Optic atrophy is seen as pale, well demarcated disc on fundoscopy. It is usually bilateral and causes a gradual loss of vision\*. Causes may be acquired or congenital

#### Acquired causes

- multiple sclerosis
- papilloedema (longstanding)
- raised intraocular pressure (e.g. glaucoma, tumour)
- retinal damage (e.g. choroiditis, retinitis pigmentosa)
- ischaemia
- toxins: tobacco amblyopia, quinine, methanol, arsenic, lead
- nutritional: vitamin B1, B2, B6 and B12 deficiency

#### Congenital causes

- Friedreich's ataxia
- mitochondrial disorders e.g. Leber's optic atrophy
- DIDMOAD - the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

\*strictly speaking optic atrophy is a descriptive term, it is the optic neuropathy that results in visual loss

A 34-year-old woman presents complaining of headaches. Examination of her pupils using a light shone alternately in each eye reveals that when the light is shone in the right eye both pupils constrict but when the light source immediately moves to the left eye both eyes appear to dilate.

What is the most likely diagnosis?

<input type="radio"/>	A. Right optic neuritis
<input type="radio"/>	B. Left sided Horner's syndrome
<input type="radio"/>	C. Craniopharyngioma
<input checked="" type="radio"/>	D. Left optic neuritis
<input type="radio"/>	E. Right Holmes-Adie pupil

Next question

This is the 'swinging light test' and reveals a relative afferent pupillary defect. As there is a defect in the afferent nerve on the left side the pupils constrict less than normal, giving the impression of dilation.

Given her age, multiple sclerosis causing optic neuritis is the likely underlying diagnosis. Optic neuritis typically causes a dull ache in the region of the eye which is aggravated by movement

### Relative afferent pupillary defect

Also known as the Marcus-Gunn pupil, a relative afferent pupillary defect is found by the 'swinging light test'. It is caused by a lesion anterior to the optic chiasm i.e. optic nerve or retina

#### Causes

- retina: detachment
- optic nerve: optic neuritis e.g. multiple sclerosis

#### Pathway of pupillary light reflex

- afferent: retina --> optic nerve --> lateral geniculate body --> midbrain
- efferent: Edinger-Westphal nucleus (midbrain) --> oculomotor nerve



**Question 6 of 54**

Next

A 65-year-old man with a known history of Paget's disease is noted to have irregular dark red lines radiating from the optic nerve. What is the likely diagnosis?

<input type="radio"/>	A. Retinitis pigmentosa
<input type="radio"/>	B. Optic neuritis
<input type="radio"/>	C. Angioid retinal streaks
<input type="radio"/>	D. Choroidoretinitis
<input type="radio"/>	E. Malignant hypertension

Next question

This is a typical description of angioid retinal streaks which are associated with Paget's disease

**Angioid retinal streaks**

Angioid retinal streaks are seen on fundoscopy as irregular dark red streaks radiating from the optic nerve head. They are caused by degeneration, calcification and breaks in Bruch's membrane .

**Causes**

- pseudoxanthoma elasticum
- Ehler-Danlos syndrome
- Paget's disease
- sickle-cell anaemia
- acromegaly

A 64-year-old woman presents with bilateral sore eyelids. She also complains of her eyes being dry all the time. On examination her eyelid margins are erythematous at the margins but are not swollen. Of the given options, what is the most appropriate initial management?

<input type="radio"/>	A. Topical chloramphenicol + mechanical removal of lid debris
<input type="radio"/>	B. Hot compresses + topical steroids
<input type="radio"/>	C. Topical chloramphenicol + topical steroids
<input type="radio"/>	D. Hot compresses + mechanical removal of lid debris
<input type="radio"/>	E. Topical chloramphenicol + hot compresses

[Next question](#)

Artificial tears may also be given for symptom relief of blepharitis

### Blepharitis

Blepharitis is inflammation of the eyelid margins. It may due to either meibomian gland dysfunction (common, posterior blepharitis) or seborrhoeic dermatitis/staphylococcal infection (less common, anterior blepharitis). Blepharitis is also more common in patients with rosacea

The meibomian glands secrete oil on to the eye surface to prevent rapid evaporation of the tear film. Any problem affecting the meibomian glands (as in blepharitis) can hence cause drying of the eyes which in turns leads to irritation

#### Features

- symptoms are usually bilateral
- grittiness and discomfort, particularly around the eyelid margins
- eyes may be sticky in the morning
- eyelid margins may be red. Swollen eyelids may be seen in staphylococcal blepharitis
- styes and chalazions are more common in patients with blepharitis
- secondary conjunctivitis may occur

#### Management

- softening of the lid margin using hot compresses twice a day
- mechanical removal of the debris from lid margins - cotton wool buds dipped in a mixture of cooled boiled water and baby shampoo is often used\*
- artificial tears may be given for symptom relief in people with dry eyes or an abnormal tear film

\*an alternative is sodium bicarbonate, a teaspoonful in a cup of cooled water that has recently been boiled

### Question 8 of 54

Next

A 67-year-old woman presents for review. She has recently been diagnosed with dry age-related macular degeneration. Which one of the following is the strongest risk factor for developing this condition?

<input type="radio"/>	A. Hypertension
<input type="radio"/>	B. Poor diet
<input type="radio"/>	C. Smoking
<input type="radio"/>	D. Diabetes mellitus
<input type="radio"/>	E. Alcohol excess

Next question

Macular degeneration - smoking is risk factor

Having a balanced diet, with plenty of fresh fruits and vegetables may also slow the progression of macular degeneration. There is still ongoing research looking at the role of supplementary antioxidants

### Age related macular degeneration

Age related macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral.

Traditionally two forms of macular degeneration are seen:

- dry (geographic atrophy) macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis

Recently there has been a move to a more updated classification:

- early age related macular degeneration (non-exudative, age related maculopathy): drusen and alterations to the retinal pigment epithelium (RPE)
- late age related macular degeneration (neovascularisation, exudative)

### Risk factors

- age: most patients are over 60 years of age
- smoking
- family history

- more common in Caucasians
- high cumulative sunlight exposure
- female sex

## Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

## Investigation and diagnosis

- optical coherence tomography: provide cross sectional views of the macula
- if neovascularisation is present fluorescein angiography is performed

## General management

- stop smoking
- high dose of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Supplements should be avoided in smokers due to an increased risk of lung cancer

## Dry macular degeneration - no current medical treatments

## Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

**Question 9 of 54**

Next

A 34-year-old man is referred to ophthalmology following a deterioration in his vision. He is noted to be tall with thin, long fingers and a degree of learning disabilities. Following review he is suspected as having a displacement of his lens on the right side. What is the most likely underlying diagnosis?

<input type="radio"/>	A. Ehlers-Danlos syndrome
<input type="radio"/>	B. Homocystinuria
<input type="radio"/>	C. Rapadilino syndrome
<input type="radio"/>	D. Marfan's syndrome
<input type="radio"/>	E. Crouzon disease

Next question

The presence of learning difficulties points to a diagnosis of homocystinuria rather than Marfan's syndrome.

**Homocystinuria**

Homocystinuria is a rare autosomal recessive disease caused by deficiency of cystathionine beta synthase. This results in an accumulation of homocysteine which is then oxidized to homocystine.

**Features**

- often patients have fine, fair hair
- musculoskeletal: may be similar to Marfan's - arachnodactyly etc
- neurological patients may have learning difficulties, seizures
- ocular: downwards (inferonasal) dislocation of lens
- increased risk of arterial and venous thromboembolism
- also malar flush, livedo reticularis

Diagnosis is made by the cyanide-nitroprusside test, which is also positive in cystinuria

Treatment is vitamin B6 (pyridoxine) supplements

A 62-year-old man presents with sudden visual loss in his right eye. He is otherwise asymptomatic. Which one of the following conditions is least likely to be responsible?

<input type="radio"/>	A. Ischaemic optic neuropathy
<input type="radio"/>	B. Occlusion of the central retinal vein
<input type="radio"/>	C. Occlusion of the central retinal artery
<input type="radio"/>	D. Optic neuritis
<input type="radio"/>	E. Vitreous haemorrhage

[Next question](#)

Whilst optic neuritis can present with sudden loss, in this 62-year-old man it is the least likely option. Typically there is a unilateral decrease in visual acuity over hours or days. There may be poor discrimination of colours and eye pain on movement

### Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

#### Ischaemic optic neuropathy

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

#### Central retinal vein occlusion

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

#### Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)

- features include afferent pupillary defect, 'cherry red' spot on a pale retina

### Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

### Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

### Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
Flashes of light (photopsia) - in the peripheral field of vision Floaters, often on the temporal side of the central vision	Dense shadow that starts peripherally progresses towards the central vision A veil or curtain over the field of vision Straight lines appear curved Central visual loss	Large bleeds cause sudden visual loss Moderate bleeds may be described as numerous dark spots Small bleeds may cause floaters

**Question 11 of 54**

Next

A 63-year-old man presents to his GP complaining of pain in his right eye. On examination the sclera is red and the pupil is dilated with a hazy cornea. What is the most likely diagnosis?

<input type="radio"/>	A. Scleritis
<input type="radio"/>	B. Conjunctivitis
<input type="radio"/>	C. Acute angle closure glaucoma
<input type="radio"/>	D. Anterior uveitis
<input type="radio"/>	E. Subconjunctival haemorrhage

Next question

Red eye - glaucoma or uveitis?

- glaucoma: severe pain, haloes, 'semi-dilated' pupil
- uveitis: small, fixed oval pupil, ciliary flush

**Red eye**

There are many possible causes of a red eye. It is important to be able to recognise the causes which require urgent referral to an ophthalmologist. Below is a brief summary of the key distinguishing features

Acute angle closure glaucoma

- severe pain (may be ocular or headache)
- decreased visual acuity, patient sees haloes
- semi-dilated pupil
- hazy cornea

Anterior uveitis

- acute onset
- pain
- blurred vision and photophobia
- small, fixed oval pupil, ciliary flush

Scleritis

- severe pain (may be worse on movement) and tenderness



- may be underlying autoimmune disease e.g. rheumatoid arthritis

### Conjunctivitis

- purulent discharge if bacterial, clear discharge if viral

### Subconjunctival haemorrhage

- history of trauma or coughing bouts

A 74-year-old man presents to ophthalmology clinic after seeing his optician. They have noticed raised intra-ocular pressure and decreased peripheral vision. His past medical history includes asthma and type 2 diabetes mellitus. What is the most appropriate treatment given the likely diagnosis?

- ☐ A. Latanoprost
- ☐ B. Pilocarpine
- ☐ C. Timolol
- ☐ D. Dorzolamide
- ☐ E. Brimonidine

Next question

A prostaglandin analogue should be used first-line in patients with a history of asthma.

### Primary open-angle glaucoma: management

The majority of patients with primary open-angle glaucoma are managed with eye drops. These aim to lower intra-ocular pressure which in turn has been shown to prevent progressive loss of visual field.

Medication	Mode of action	Notes
Prostaglandin analogues (e.g. Latanoprost)	Increases uveoscleral outflow	Once daily administration  Adverse effects include brown pigmentation of the iris
Beta-blockers (e.g. Timolol)	Reduces aqueous production	Should be avoided in asthmatics and patients with heart block
Sympathomimetics (e.g. Brimonidine, an alpha2-adrenoceptor agonist)	Reduces aqueous production and increases outflow	Avoid if taking MAOI or tricyclic antidepressants  Adverse effects include hyperaemia
Carbonic anhydrase inhibitors (e.g. Dorzolamide)	Reduces aqueous production	Systemic absorption may cause sulphonamide-like reactions
Miotics (e.g. Pilocarpine)	Increases uveoscleral outflow	Adverse effects included a constricted pupil, headache and blurred vision

Surgery in the form of a trabeculectomy may be considered in refractory cases.

**Question 13 of 54**

Next

A 54-year-old woman presents with a persistent watery left eye for the past 4 days. On examination there is erythema and swelling of the inner canthus of the left eye. What is the most likely diagnosis?

<input type="radio"/>	A. Blepharitis
<input type="radio"/>	B. Acute angle closure glaucoma
<input type="radio"/>	C. Meibomian cyst
<input type="radio"/>	D. Dacryocystitis
<input type="radio"/>	E. Pinguecula

Next question

**Lacrimal duct problems**

**Dacryocystitis** is infection of the lacrimal sac

Features

- watering eye (epiphora)
- swelling and erythema at the inner canthus of the eye

Management is with systemic antibiotics. Intravenous antibiotics are indicated if there is associated periorbital cellulitis

**Congenital lacrimal duct obstruction** affects around 5-10% of newborns. It is bilateral in around 20% of cases

Features

- watering eye (even if not crying)
- secondary infection may occur

Symptoms resolve in 99% of cases by 12 months of age

**Question 14 of 54**

Next

A 71-year-old man presents with severe pain around his right eye and vomiting. On examination the right eye is red and decreased visual acuity is noted. Which one of the following options is the most appropriate initial treatment?

<input type="radio"/>	A. Topical pilocarpine + oral prednisolone
<input type="radio"/>	B. Topical pilocarpine + topical steroids
<input type="radio"/>	C. Topical steroids
<input type="radio"/>	D. Topical pilocarpine + intravenous acetazolamide
<input type="radio"/>	E. Topical steroids + intravenous acetazolamide

Next question

Treatment of acute glaucoma - acetazolamide + pilocarpine

**Acute angle closure glaucoma**

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

In acute angle closure glaucoma (AACG) there is a rise in IOP secondary to an impairment of aqueous outflow. Factors predisposing to AACG include:

- hypermetropia (long-sightedness)
- pupillary dilatation
- lens growth associated with age

**Features**

- severe pain: may be ocular or headache
- decreased visual acuity
- symptoms worse with mydriasis (e.g. watching TV in a dark room)
- hard, red eye
- haloes around lights
- semi-dilated non-reacting pupil
- corneal oedema results in dull or hazy cornea
- systemic upset may be seen, such as nausea and vomiting and even abdominal pain

## Management

- urgent referral to an ophthalmologist
- management options include reducing aqueous secretions with acetazolamide and inducing pupillary constriction with topical pilocarpine

**Question 15 of 54**

Next

A 35-year-old man presents with visual problems. He has had very poor vision in the dark for a long time but is now worried as he is developing 'tunnel vision'. He states his grandfather had a similar problem and was registered blind in his 50's. What is the most likely diagnosis?

<input type="radio"/>	A. Leber's congenital amaurosis
<input type="radio"/>	B. Vitelliform macular dystrophy
<input type="radio"/>	C. Central serous retinopathy
<input type="radio"/>	D. Primary open angle glaucoma
<input type="radio"/>	E. Retinitis pigmentosa

Next question

Retinitis pigmentosa - night blindness + funnel vision

**Retinitis pigmentosa**

Retinitis pigmentosa primarily affects the peripheral retina resulting in funnel vision

**Features**

- night blindness is often the initial sign
- funnel vision (the preferred term for tunnel vision)
- fundoscopy: black bone spicule-shaped pigmentation in the peripheral retina, mottling of the retinal pigment epithelium

**Associated diseases**

- Refsum disease: cerebellar ataxia, peripheral neuropathy, deafness, ichthyosis
- Usher syndrome
- abetalipoproteinemia
- Lawrence-Moon-Biedl syndrome
- Kearns-Sayre syndrome
- Alport's syndrome

Each one of the following is associated with retinitis pigmentosa, except:

<input type="radio"/>	A. Usher syndrome
<input type="radio"/>	B. Refsum disease
<input type="radio"/>	C. Kearns-Sayre syndrome
<input type="radio"/>	D. Tuberous sclerosis
<input type="radio"/>	E. Abetalipoproteinaemia

[Next question](#)

Ocular manifestations of tuberose sclerosis includes retinal hamartomas

### Retinitis pigmentosa

Retinitis pigmentosa primarily affects the peripheral retina resulting in funnel vision

#### Features

- night blindness is often the initial sign
- funnel vision (the preferred term for tunnel vision)
- fundoscopy: black bone spicule-shaped pigmentation in the peripheral retina, mottling of the retinal pigment epithelium

#### Associated diseases

- Refsum disease: cerebellar ataxia, peripheral neuropathy, deafness, ichthyosis
- Usher syndrome
- abetalipoproteinemia
- Lawrence-Moon-Biedl syndrome
- Kearns-Sayre syndrome
- Alport's syndrome

A 60-year-old woman who has recently started treatment for polymyalgia rheumatica presents with a five day history of headaches and reduced vision on the right side since this morning. There is no eye pain but there is a 'large, dark shadow' covering the superior visual field on the right side. On examination she has a tender, palpable right temporal artery. What is the most likely explanation for the reduced vision?

- ☐ A. Anterior ischemic optic neuropathy
- ☐ B. Central retinal vein occlusion
- ☐ C. Optic neuritis
- ☐ D. Ophthalmic arteritis
- ☐ E. Central retinal artery occlusion

[Next question](#)

### Temporal arteritis

Temporal arteritis is large vessel vasculitis which overlaps with polymyalgia rheumatica (PMR). Histology shows changes which characteristically 'skips' certain sections of affected artery whilst damaging others.

#### Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- headache (found in 85%)
- jaw claudication (65%)
- visual disturbances secondary to anterior ischemic optic neuropathy
- tender, palpable temporal artery
- features of PMR: aching, morning stiffness in proximal limb muscles (not weakness)
- also lethargy, depression, low-grade fever, anorexia, night sweats

#### Investigations

- raised inflammatory markers: ESR > 50 mm/hr (note ESR < 30 in 10% of patients). CRP may also be elevated
- temporal artery biopsy: skip lesions may be present
- note creatine kinase and EMG normal

#### Treatment

- high-dose prednisolone - there should be a dramatic response, if not the diagnosis should be reconsidered
- urgent ophthalmology review. Patients with visual symptoms should be seen the same-day by an ophthalmologist. Visual damage is often irreversible



Which one of the following statements regarding macular degeneration is true?

<input type="radio"/>	A. Drusen are characteristic of wet macular degeneration
<input type="radio"/>	B. Photodynamic therapy is useful in dry macular degeneration
<input type="radio"/>	C. Asian ethnicity is a risk factor
<input type="radio"/>	D. Male sex is a risk factor
<input type="radio"/>	E. Wet macular degeneration carries the worst prognosis

Next question

### Age related macular degeneration

Age related macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral.

Traditionally two forms of macular degeneration are seen:

- dry (geographic atrophy) macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis

Recently there has been a move to a more updated classification:

- early age related macular degeneration (non-exudative, age related maculopathy): drusen and alterations to the retinal pigment epithelium (RPE)
- late age related macular degeneration (neovascularisation, exudative)

Risk factors

- age: most patients are over 60 years of age
- smoking
- family history
- more common in Caucasians
- high cumulative sunlight exposure
- female sex

Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

#### Investigation and diagnosis

- optical coherence tomography: provide cross sectional views of the macula
- if neovascularisation is present fluorescein angiography is performed

#### General management

- stop smoking
- high dose of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Supplements should be avoided in smokers due to an increased risk of lung cancer

#### Dry macular degeneration - no current medical treatments

#### Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

Which one of the following is least associated with the development of optic atrophy?

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Tobacco                |
| <input type="radio"/> | B. Methanol               |
| <input type="radio"/> | C. Vitamin B12 deficiency |
| <input type="radio"/> | D. Lead                   |
| <input type="radio"/> | E. Zinc deficiency        |

Next question

### Optic atrophy

Optic atrophy is seen as pale, well demarcated disc on fundoscopy. It is usually bilateral and causes a gradual loss of vision\*. Causes may be acquired or congenital

#### Acquired causes

- multiple sclerosis
- papilloedema (longstanding)
- raised intraocular pressure (e.g. glaucoma, tumour)
- retinal damage (e.g. choroiditis, retinitis pigmentosa)
- ischaemia
- toxins: tobacco amblyopia, quinine, methanol, arsenic, lead
- nutritional: vitamin B1, B2, B6 and B12 deficiency

#### Congenital causes

- Friedreich's ataxia
- mitochondrial disorders e.g. Leber's optic atrophy
- DIDMOAD - the association of cranial Diabetes Insipidus, Diabetes Mellitus, Optic Atrophy and Deafness (also known as Wolfram's syndrome)

\*strictly speaking optic atrophy is a descriptive term, it is the optic neuropathy that results in visual loss

Which one of the following causes of Horner's syndrome is due to a central lesion?

- ☐ A. Cavernous sinus thrombosis
- ☐ B. Internal carotid aneurysm
- ☐ C. Syringomyelia
- ☐ D. Pancoast's tumour
- ☐ E. Cervical rib

Next question

Horner's syndrome - anhydrosis determines site of lesion:

- head, arm, trunk = central lesion: stroke, syringomyelia
- just face = pre-ganglionic lesion: Pancoast's, cervical rib
- absent = post-ganglionic lesion: carotid artery

## Horner's syndrome

### Features

- miosis (small pupil)
- ptosis
- enophthalmos\* (sunken eye)
- anhydrosis (loss of sweating one side)

### Distinguishing between causes

- heterochromia (difference in iris colour) is seen in congenital Horner's
- anhydrosis: see below

Central lesions	Pre-ganglionic lesions	Post-ganglionic lesions
Anhydrosis of the face, arm and trunk	Anhydrosis of the face	No anhydrosis
Stroke Syringomyelia Multiple sclerosis Tumour Encephalitis	Pancoast's tumour Thyroidectomy Trauma Cervical rib	Carotid artery dissection Carotid aneurysm Cavernous sinus thrombosis Cluster headache

\*in reality the appearance is due to a narrow palpebral aperture rather than true enophthalmos

A 68-year-old man with a history of type 2 diabetes mellitus presents with worsening eye sight. Mydriatic drops are applied and fundoscopy reveals pre-proliferative diabetic retinopathy. A referral to ophthalmology is made. Later in the evening whilst driving home he develops pain in his left eye associated with decreased visual acuity. What is the most likely diagnosis?

<input type="radio"/>	A. Keratitis secondary to mydriatic drops
<input type="radio"/>	B. Proliferative diabetic retinopathy
<input type="radio"/>	C. Acute angle closure glaucoma
<input type="radio"/>	D. Central retinal artery occlusion
<input type="radio"/>	E. Vitreous haemorrhage

Mydriatic drops are a known precipitant of acute angle closure glaucoma. This scenario is more common in exams than clinical practice.

### Acute angle closure glaucoma

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

In acute angle closure glaucoma (AACG) there is a rise in IOP secondary to an impairment of aqueous outflow. Factors predisposing to AACG include:

- hypermetropia (long-sightedness)
- pupillary dilatation
- lens growth associated with age

#### Features

- severe pain: may be ocular or headache
- decreased visual acuity
- symptoms worse with mydriasis (e.g. watching TV in a dark room)
- hard, red eye
- haloes around lights
- semi-dilated non-reacting pupil
- corneal oedema results in dull or hazy cornea
- systemic upset may be seen, such as nausea and vomiting and even abdominal pain

#### Management

- urgent referral to an ophthalmologist
- management options include reducing aqueous secretions with acetazolamide and inducing pupillary constriction with topical pilocarpine

**Question 22 of 54**

Next

A 71-year-old with a history of type 2 diabetes mellitus and hypertension presents due to the sensation of light flashes in his right eye. These symptoms have been present for the past 2 days and seem to occur more at the peripheral part of vision. There is no redness or pain in the affected eye. Corrected visual acuity is measured as 6/9 in both eyes. What is the most likely diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Change in shape of eye secondary to variations in blood sugar |
| <input type="radio"/> | B. Primary open angle glaucoma                                   |
| <input type="radio"/> | C. Vitreous detachment   |
| <input type="radio"/> | D. Normal phenomenon in diabetic retinopathy                     |
| <input type="radio"/> | E. Normal phenomenon in healthy eyes                             |

Next question

Flashes and floaters - vitreous/retinal detachment

Flashes and floaters are symptoms of vitreous detachment. The patient is at risk of retinal detachment and should be referred urgently to an ophthalmologist

**Sudden painless loss of vision**

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

**Ischaemic optic neuropathy**

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

**Central retinal vein occlusion**

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

## Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)
- features include afferent pupillary defect, 'cherry red' spot on a pale retina

## Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

## Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

## Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
Flashes of light (photopsia) - in the peripheral field of vision Floaters, often on the temporal side of the central vision	Dense shadow that starts peripherally progresses towards the central vision A veil or curtain over the field of vision Straight lines appear curved Central visual loss	Large bleeds cause sudden visual loss Moderate bleeds may be described as numerous dark spots Small bleeds may cause floaters

A 67-year-old man presents as he has developed a painful blistering rash around his right eye. On examination a vesicular rash covering the right trigeminal nerve dermatome is seen. Currently he has no eye symptoms or signs. Which one of the following is most likely to predict future eye involvement?

<input type="radio"/>	A. Presence of the rash on the tip of his nose
<input type="radio"/>	B. Smoking history
<input type="radio"/>	C. Increasing age
<input type="radio"/>	D. Previous courses of corticosteroids
<input type="radio"/>	E. Presence of the rash in the ear canal

[Next question](#)

This is Hutchinson's sign which is strongly predictive for ocular involvement.

### Herpes zoster ophthalmicus

Herpes zoster ophthalmicus (HZO) describes the reactivation of the varicella zoster virus in the area supplied by the ophthalmic division of the trigeminal nerve. It accounts for around 10% of case of shingles.

#### Features

- vesicular rash around the eye, which may or may not involve the actual eye itself
- Hutchinson's sign: rash on the tip or side of the nose. Indicates nasociliary involvement and is a strong risk factor for ocular involvement

#### Management

- oral antiviral treatment for 7-10 days, ideally started within 72 hours. Topical antiviral treatment is not given in HZO
- oral corticosteroids may reduce the duration of pain but do not reduce the incidence of post-herpetic neuralgia
- ocular involvement requires urgent ophthalmology review

#### Complications

- ocular: conjunctivitis, keratitis, episcleritis, anterior uveitis
- ptosis
- post-herpetic neuralgia



Each one of the following is a cause of a mydriatic pupil, except:

<input type="radio"/>	A. Third nerve palsy
<input type="radio"/>	B. Atropine
<input type="radio"/>	C. Holmes-Adie pupil
<input type="radio"/>	D. Argyll-Robertson pupil
<input type="radio"/>	E. Traumatic iridoplegia

Next question

Argyll-Robertson pupil is one of the classic pupillary syndrome. It is sometimes seen in neurosyphilis and is often said to be the prostitute's pupil - accommodates but doesn't react. Another mnemonic used for the Argyll-Robertson Pupil (ARP) is Accommodation Reflex Present (ARP) but Pupillary Reflex Absent (PRA)

#### Features

- small, irregular pupils
- no response to light but there is a response to accommodate

#### Causes

- diabetes mellitus
- syphilis

### Mydriasis

#### Causes of mydriasis (large pupil)

- third nerve palsy
- Holmes-Adie pupil
- traumatic iridoplegia
- phaeochromocytoma
- congenital

#### Drug causes of mydriasis

- topical mydriatics: tropicamide, atropine
- sympathomimetic drugs: amphetamines, cocaine
- anticholinergic drugs: tricyclic antidepressants

A 45-year-old woman with Graves' disease comes for review. She has recently been diagnosed with thyroid eye disease and is being considered for radiotherapy. Over the past three days her right eye has become red and painful. On examination there is proptosis and erythema of the right eye. Visual acuity is 6/9 in both eyes. What complication is she most likely to have developed?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Exposure keratopathy             |
| <input type="radio"/> | B. Optic neuropathy                 |
| <input type="radio"/> | C. Carbimazole-related neutropaenia |
| <input type="radio"/> | D. Central retinal vein occlusion   |
| <input type="radio"/> | E. Sjogren's Syndrome               |

Next question

### Thyroid eye disease

Thyroid eye disease affects between 25-50% of patients with Graves' disease. It is thought to be caused by an autoimmune response against an autoantigen, possibly the TSH receptor, which in turns causes retro-orbital inflammation. The patient may be eu-, hypo- or hyperthyroid at the time of presentation

#### Prevention

- smoking is the most important modifiable risk factor for the development of thyroid eye disease
- radioiodine treatment may increase the inflammatory symptoms seen in thyroid eye disease. In a recent study of patients with Graves' disease around 15% developed, or had worsening of, eye disease. Prednisolone may help reduce the risk

#### Features

- exophthalmos
- conjunctival oedema
- optic disc swelling
- ophthalmoplegia
- inability to close the eye lids may lead to sore, dry eyes. If severe and untreated patients can be at risk of exposure keratopathy

#### Management

- topical lubricants may be needed to help prevent corneal inflammation caused by exposure
- steroids
- radiotherapy
- surgery

Each one of the following are associated with angioid retinal streaks, except:

<input type="radio"/>	A. Paget's disease
<input type="radio"/>	B. Pseudoxanthoma elasticum
<input type="radio"/>	C. Acromegaly
<input type="radio"/>	D. Kearns-Sayre syndrome
<input type="radio"/>	E. Ehler-Danlos syndrome

Next question

Kearns-Sayre syndrome is a mitochondrial disorder associated with retinitis pigmentosa

### Angioid retinal streaks

Angioid retinal streaks are seen on fundoscopy as irregular dark red streaks radiating from the optic nerve head. They are caused by degeneration, calcification and breaks in Bruch's membrane .

#### Causes

- pseudoxanthoma elasticum
- Ehler-Danlos syndrome
- Paget's disease
- sickle-cell anaemia
- acromegaly

Which one of the following is not a risk factor for primary open-angle glaucoma?

- |                       |                             |
|-----------------------|-----------------------------|
| <input type="radio"/> | A. Diabetes mellitus        |
| <input type="radio"/> | B. Family history           |
| <input type="radio"/> | C. Hypertension             |
| <input type="radio"/> | D. Afro-Caribbean ethnicity |
| <input type="radio"/> | E. Hypermetropia            |

Next question

Acute angle closure glaucoma is associated with hypermetropia, where as primary open-angle glaucoma is associated with myopia

### Primary open-angle glaucoma

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

Primary open-angle glaucoma (POAG, also referred to as chronic simple glaucoma) is present in around 2% of people older than 40 years. Other than age, risk factors include:

- family history
- black patients
- myopia
- hypertension
- diabetes mellitus

POAG may present insidiously and for this reason is often detected during routine optometry appointments. Features may include

- peripheral visual field loss - nasal scotomas progressing to 'tunnel vision'
- decreased visual acuity
- optic disc cupping

**Question 28 of 54**

Next

A 23-year-old female presents with recurrent headaches. Examination of her cranial nerves reveals the right pupil is 3 mm whilst the left pupil is 5 mm. The right pupil constricts to light but the left pupil is sluggish. What is the most likely diagnosis?

<input type="radio"/>	A. Horner's syndrome
<input type="radio"/>	B. Migraine
<input type="radio"/>	C. Multiple sclerosis
<input type="radio"/>	D. Holmes-Adie syndrome
<input type="radio"/>	E. Argyll-Roberson syndrome

Next question

Holmes ADie = DIlated pupil, females, absent leg reflexes

**Holmes-Adie pupil**

Holmes-Adie pupil is a benign condition most commonly seen in women. It is one of the differentials of a dilated pupil.

**Overview**

- unilateral in 80% of cases
- dilated pupil
- once the pupil has constricted it remains small for an abnormally long time
- slowly reactive to accommodation but very poorly (if at all) to light

**Holmes-Adie syndrome**

- association of Holmes-Adie pupil with absent ankle/knee reflexes

A 70-year-old man is investigated for blurred vision. Fundoscopy reveals drusen, retinal epithelial and macular neovascularisation. A diagnosis of age related macular degeneration is suspected. What is the most appropriate next investigation?

<input type="radio"/>	A. Vitreous fluid sampling
<input type="radio"/>	B. MRI orbits
<input type="radio"/>	C. Ocular tonometry
<input checked="" type="radio"/>	D. Fluorescein angiography
<input type="radio"/>	E. Kinetic perimetry

[Next question](#)

### Age related macular degeneration

Age related macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral.

Traditionally two forms of macular degeneration are seen:

- dry (geographic atrophy) macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis

Recently there has been a move to a more updated classification:

- early age related macular degeneration (non-exudative, age related maculopathy): drusen and alterations to the retinal pigment epithelium (RPE)
- late age related macular degeneration (neovascularisation, exudative)

### Risk factors

- age: most patients are over 60 years of age
- smoking
- family history
- more common in Caucasians
- high cumulative sunlight exposure
- female sex

## Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

## Investigation and diagnosis

- optical coherence tomography: provide cross sectional views of the macula
- if neovascularisation is present fluorescein angiography is performed

## General management

- stop smoking
- high dose of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Supplements should be avoided in smokers due to an increased risk of lung cancer

## Dry macular degeneration - no current medical treatments

## Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

During routine follow-up at renal clinic a man is noted to have corpuscular pigmentation of the left retina. Which one of the following conditions is associated with retinitis pigmentosa?

<input type="radio"/>	A. Autosomal dominant polycystic kidney disease
<input type="radio"/>	B. Tuberous sclerosis
<input type="radio"/>	C. Von Hippel-Lindau syndrome
<input type="radio"/>	D. Alport's syndrome
<input type="radio"/>	E. Medullary sponge kidney

[Next question](#)

### Retinitis pigmentosa

Retinitis pigmentosa primarily affects the peripheral retina resulting in funnel vision

#### Features

- night blindness is often the initial sign
- funnel vision (the preferred term for tunnel vision)
- fundoscopy: black bone spicule-shaped pigmentation in the peripheral retina, mottling of the retinal pigment epithelium

#### Associated diseases

- Refsum disease: cerebellar ataxia, peripheral neuropathy, deafness, ichthyosis
- Usher syndrome
- abetalipoproteinemia
- Lawrence-Moon-Biedl syndrome
- Kearns-Sayre syndrome
- Alport's syndrome



An 84-year-old man presents with loss of vision in his left eye since the morning. He is otherwise asymptomatic and of note has had no associated eye pain or headaches. His past medical history includes ischaemic heart disease but he is otherwise well. On examination he has no vision in his left eye. The left pupil responds poorly to light but the consensual light reaction is normal. Fundoscopy reveals a red spot over a pale and opaque retina. What is the most likely diagnosis?

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Vitreous haemorrhage             |
| <input type="radio"/> | B. Retinal detachment               |
| <input type="radio"/> | C. Ischaemic optic neuropathy       |
| <input type="radio"/> | D. Central retinal vein occlusion   |
| <input type="radio"/> | E. Central retinal artery occlusion |

[Next question](#)

### Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

#### Ischaemic optic neuropathy

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

#### Central retinal vein occlusion

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

#### Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)
- features include afferent pupillary defect, 'cherry red' spot on a pale retina

#### Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

#### Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

#### Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
Flashes of light (photopsia) - in the peripheral field of vision Floaters, often on the temporal side of the central vision	Dense shadow that starts peripherally progresses towards the central vision A veil or curtain over the field of vision Straight lines appear curved Central visual loss	Large bleeds cause sudden visual loss Moderate bleeds may be described as numerous dark spots Small bleeds may cause floaters

**Question 32 of 54**[Next](#)

Which one of the following is least recognised as a cause of tunnel vision?

- |                       |                            |
|-----------------------|----------------------------|
| <input type="radio"/> | A. Papilloedema            |
| <input type="radio"/> | B. Choroidoretinitis       |
| <input type="radio"/> | C. Angioid retinal streaks |
| <input type="radio"/> | D. Glaucoma                |
| <input type="radio"/> | E. Retinitis pigmentosa    |

[Next question](#)**Tunnel vision**

Tunnel vision is the concentric diminution of the visual fields

**Causes**

- papilloedema
- glaucoma
- retinitis pigmentosa
- choroidoretinitis
- optic atrophy secondary to tabes dorsalis
- hysteria

A 70-year-old woman presents with loss of vision in her left eye. For the past two weeks she has painful frontal headaches and has been feeling generally lethargic. On examination visual acuity is 6/9 in the right eye but on the left side only hand movements can be made seen. Fundoscopy of the left side reveals a pale and oedematous optic disc. What is the most likely diagnosis?.

- |                       |                                     |
|-----------------------|-------------------------------------|
| <input type="radio"/> | A. Acute angle closure glaucoma     |
| <input type="radio"/> | B. Central retinal artery occlusion |
| <input type="radio"/> | C. Multiple sclerosis               |
| <input type="radio"/> | D. Methanol poisoning               |
| <input type="radio"/> | E. Temporal arteritis               |

[Next question](#)

This patient has likely developed anterior ischemic optic neuropathy on the left side

### Temporal arteritis

Temporal arteritis is large vessel vasculitis which overlaps with polymyalgia rheumatica (PMR). Histology shows changes which characteristically 'skips' certain sections of affected artery whilst damaging others.

#### Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- headache (found in 85%)
- jaw claudication (65%)
- visual disturbances secondary to anterior ischemic optic neuropathy
- tender, palpable temporal artery
- features of PMR: aching, morning stiffness in proximal limb muscles (not weakness)
- also lethargy, depression, low-grade fever, anorexia, night sweats

#### Investigations

- raised inflammatory markers: ESR > 50 mm/hr (note ESR < 30 in 10% of patients). CRP may also be elevated
- temporal artery biopsy: skip lesions may be present
- note creatine kinase and EMG normal

#### Treatment

- high-dose prednisolone - there should be a dramatic response, if not the diagnosis should be reconsidered
- urgent ophthalmology review. Patients with visual symptoms should be seen the same-day by an ophthalmologist. Visual damage is often irreversible

A 52-year-old old man who has a history of alcohol excess is brought to the Emergency Department by paramedics. He is a frequent attender and this time has a laceration on his scalp following a fall. Whilst examining him he seems confused and complains of problems with his vision. Which one of the following is the most commonly found ocular abnormality in patients with Wernicke's encephalopathy?

- |                       |                         |
|-----------------------|-------------------------|
| <input type="radio"/> | A. Ophthalmoplegia      |
| <input type="radio"/> | B. Lateral rectus palsy |
| <input type="radio"/> | C. Nystagmus            |
| <input type="radio"/> | D. Mydriasis            |
| <input type="radio"/> | E. Scotomata            |

[Next question](#)

### Wernicke's encephalopathy

Wernicke's encephalopathy is a neuropsychiatric disorder caused by thiamine deficiency which is most commonly seen in alcoholics. Rarer causes include: persistent vomiting, stomach cancer, dietary deficiency. A classic triad of nystagmus, ophthalmoplegia and ataxia may occur. In Wernicke's encephalopathy petechial haemorrhages occur in a variety of structures in the brain including the mamillary bodies and ventricle walls

#### Features

- nystagmus (the most common ocular sign)
- ophthalmoplegia
- ataxia
- confusion, altered GCS
- peripheral sensory neuropathy

#### Investigations

- decreased red cell transketolase
- MRI

Treatment is with urgent replacement of thiamine

Which one of the following is not a feature of background diabetic retinopathy?

- ☐ A. Microaneurysms
- ☐ B. Blot haemorrhages
- ☐ C. Cotton wool spots
- ☐ D. Seen in both type 1 and type 2 diabetes mellitus
- ☐ E. Hard exudates

Next question

Cotton wool spots are seen in pre-proliferative retinopathy

### Diabetic retinopathy

Diabetic retinopathy is the most common cause of blindness in adults aged 35-65 years-old. Hyperglycaemia is thought to cause increased retinal blood flow and abnormal metabolism in the retinal vessel walls. This precipitates damage to endothelial cells and pericytes

Endothelial dysfunction leads to increased vascular permeability which causes the characteristic exudates seen on fundoscopy. Pericyte dysfunction predisposes to the formation of microaneurysms. Neovascularization is thought to be caused by the production of growth factors in response to retinal ischaemia

In exams you are most likely to be asked about the characteristic features of the various stages/types of diabetic retinopathy. Recently a new classification system has been proposed, dividing patients into those with non-proliferative diabetic retinopathy (NPDR) and those with proliferative retinopathy (PDR):

Traditional classification	New classification
Background retinopathy <ul style="list-style-type: none"> <li>microaneurysms (dots)</li> <li>blot haemorrhages (<math>\leq 3</math>)</li> <li>hard exudates</li> </ul>	Mild NPDR <ul style="list-style-type: none"> <li>1 or more microaneurysm</li> </ul>
Pre-proliferative retinopathy <ul style="list-style-type: none"> <li>cotton wool spots (soft exudates; ischaemic nerve fibres)</li> <li>&gt; 3 blot haemorrhages</li> <li>venous beading/looping</li> <li>deep/dark cluster haemorrhages</li> <li>more common in Type I DM, treat with laser photocoagulation</li> </ul>	Moderate NPDR <ul style="list-style-type: none"> <li>microaneurysms</li> <li>blot haemorrhages</li> <li>hard exudates</li> <li>cotton wool spots, venous beading/looping and intraretinal microvascular abnormalities (IRMA) less severe than in severe NPDR</li> </ul>
	Severe NPDR <ul style="list-style-type: none"> <li>blot haemorrhages and microaneurysms in 4 quadrants</li> <li>venous beading in at least 2 quadrants</li> <li>IRMA in at least 1 quadrant</li> </ul>

## Proliferative retinopathy

- retinal neovascularisation - may lead to vitreous haemorrhage
- fibrous tissue forming anterior to retinal disc
- more common in Type I DM, 50% blind in 5 years

## Maculopathy

- based on location rather than severity, anything is potentially serious
- hard exudates and other 'background' changes on macula
- check visual acuity
- more common in Type II DM

Each one of the following predisposes to cataract formation, except:

<input type="radio"/>	A. Down's syndrome
<input type="radio"/>	B. Hypercalcaemia
<input type="radio"/>	C. Diabetes mellitus
<input type="radio"/>	D. Long-term steroid use
<input type="radio"/>	E. Uveitis

Next question

## Cataracts

### Majority

- age related
- UV light

### Systemic

- diabetes mellitus
- steroids
- infection (congenital rubella)
- metabolic (hypocalcaemia, galactosaemia)
- myotonic dystrophy, Down's syndrome

### Ocular

- trauma
- uveitis
- high myopia
- topical steroids

### Classification

- Nuclear: change lens refractive index, common in old age
- Polar: localized, commonly inherited, lie in the visual axis
- Subcapsular: due to steroid use, just deep to the lens capsule, in the visual axis
- Dot opacities: common in normal lenses, also seen in diabetes and myotonic dystrophy



A 65-year-old woman presents to the Emergency Department with visual problems. She has rheumatoid arthritis, depression and takes medication to control her blood pressure. Over the past few days she has been getting troublesome headaches and blurred vision but today has noted a marked reduction in vision in the right eye. On examination her right eye is red, has a sluggish pupil and a corrected visual acuity 6/30. Her medication has recently been changed. Which one of the following drugs is most likely to have precipitated this event?

<input type="radio"/>	A. Methotrexate
<input type="radio"/>	B. Doxazosin
<input type="radio"/>	C. Amitriptyline
<input type="radio"/>	D. Atenolol
<input type="radio"/>	E. Bendroflumethiazide

Drugs which may precipitate acute glaucoma include anticholinergics and tricyclic antidepressants

### Acute angle closure glaucoma

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

In acute angle closure glaucoma (AACG) there is a rise in IOP secondary to an impairment of aqueous outflow. Factors predisposing to AACG include:

- hypermetropia (long-sightedness)
- pupillary dilatation
- lens growth associated with age

### Features

- severe pain: may be ocular or headache
- decreased visual acuity
- symptoms worse with mydriasis (e.g. watching TV in a dark room)
- hard, red eye
- haloes around lights
- semi-dilated non-reacting pupil
- corneal oedema results in dull or hazy cornea
- systemic upset may be seen, such as nausea and vomiting and even abdominal pain

### Management

- urgent referral to an ophthalmologist
- management options include reducing aqueous secretions with acetazolamide and inducing pupillary constriction with topical pilocarpine

Which one of the following is associated with heterochromia in congenital disease?

<input type="radio"/>	A. Holmes-Adie pupil
<input type="radio"/>	B. Third nerve palsy
<input type="radio"/>	C. Sixth nerve palsy
<input type="radio"/>	D. Argyll-Robertson pupil
<input type="radio"/>	E. Horner's syndrome

Next question

## Horner's syndrome

### Features

- miosis (small pupil)
- ptosis
- enophthalmos\* (sunken eye)
- anhydrosis (loss of sweating one side)

### Distinguishing between causes

- heterochromia (difference in iris colour) is seen in congenital Horner's
- anhydrosis: see below

Central lesions	Pre-ganglionic lesions	Post-ganglionic lesions
Anhydrosis of the face, arm and trunk	Anhydrosis of the face	No anhydrosis
Stroke Syringomyelia Multiple sclerosis Tumour Encephalitis	Pancoast's tumour Thyroidectomy Trauma Cervical rib	Carotid artery dissection Carotid aneurysm Cavernous sinus thrombosis Cluster headache

\*in reality the appearance is due to a narrow palpebral aperture rather than true enophthalmos

A 64-year-old woman with type 2 diabetes mellitus presents as she has started to bump into things since the morning. Over the previous two days she had noticed some 'floating spots in her eyes'. Examination reveals she has no vision in her right eye. The red reflex on the right side is difficult to elicit and you are unable to visualise the retina on the right side during fundoscopy. Examination of the left fundus reveals changes consistent with pre-proliferative diabetic retinopathy. What is the most likely diagnosis?

<input type="radio"/>	A. Occlusion of central retinal vein
<input type="radio"/>	B. Vitreous haemorrhage
<input type="radio"/>	C. Proliferative retinopathy
<input type="radio"/>	D. Cataract
<input type="radio"/>	E. Retinal detachment

[Next question](#)

The history of diabetes, complete loss of vision in the affected eye and inability to visualise the retina point towards a diagnosis of vitreous haemorrhage. Please see the table below for help in differentiating retinal detachment from vitreous haemorrhage.

### Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

#### Ischaemic optic neuropathy

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

#### Central retinal vein occlusion

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

## Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)
- features include afferent pupillary defect, 'cherry red' spot on a pale retina

## Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

## Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

## Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
Flashes of light (photopsia) - in the peripheral field of vision Floaters, often on the temporal side of the central vision	Dense shadow that starts peripherally progresses towards the central vision A veil or curtain over the field of vision Straight lines appear curved Central visual loss	Large bleeds cause sudden visual loss Moderate bleeds may be described as numerous dark spots Small bleeds may cause floaters

A 72-year-old woman presents with a vesicular rash around her left eye. The left eye is red and there is a degree of photophobia. A presumptive diagnosis of herpes zoster ophthalmicus is made and an urgent referral to ophthalmology is made. What treatment is she most likely to be given?

<input type="radio"/>	A. Oral aciclovir + topical aciclovir
<input type="radio"/>	B. Intravenous aciclovir + topical aciclovir
<input type="radio"/>	C. Oral famciclovir + topical aciclovir
<input type="radio"/>	D. Topical aciclovir
<input type="radio"/>	E. Oral aciclovir

[Next question](#)

## Herpes zoster ophthalmicus

Herpes zoster ophthalmicus (HZO) describes the reactivation of the varicella zoster virus in the area supplied by the ophthalmic division of the trigeminal nerve. It accounts for around 10% of case of shingles.

### Features

- vesicular rash around the eye, which may or may not involve the actual eye itself
- Hutchinson's sign: rash on the tip or side of the nose. Indicates nasociliary involvement and is a strong risk factor for ocular involvement

### Management

- oral antiviral treatment for 7-10 days, ideally started within 72 hours. Topical antiviral treatment is not given in HZO
- oral corticosteroids may reduce the duration of pain but do not reduce the incidence of post-herpetic neuralgia
- ocular involvement requires urgent ophthalmology review

### Complications

- ocular: conjunctivitis, keratitis, episcleritis, anterior uveitis
- ptosis
- post-herpetic neuralgia

An 80-year-old woman presents with 'funny spots' affecting her vision. Over the past week she has noticed a number of flashes and floaters in the visual field of the right eye. What is the most likely diagnosis?

<input type="radio"/>	A. Retinal detachment
<input type="radio"/>	B. Posterior vitreous detachment
<input type="radio"/>	C. Optic neuritis
<input type="radio"/>	D. Depression
<input type="radio"/>	E. Vitreous haemorrhage

[Next question](#)

Posterior vitreous detachment is thought to occur in up to 50-75% of the population over 65 years and is the most likely diagnosis here. Such patients are normally reviewed by an ophthalmologist to assess the risk of progressing to retinal detachment.

### Sudden painless loss of vision

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
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#### Ischaemic optic neuropathy

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
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- altitudinal field defects are seen

#### Central retinal vein occlusion

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

#### Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)

- features include afferent pupillary defect, 'cherry red' spot on a pale retina

### Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

### Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

### Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
Flashes of light (photopsia) - in the peripheral field of vision Floaters, often on the temporal side of the central vision	Dense shadow that starts peripherally progresses towards the central vision A veil or curtain over the field of vision Straight lines appear curved Central visual loss	Large bleeds cause sudden visual loss Moderate bleeds may be described as numerous dark spots Small bleeds may cause floaters

A 71-year-old female with dry age-related macular degeneration is reviewed. Unfortunately her eyesight has deteriorated over the past six months. She has never smoked and is taking antioxidant supplements. What is the most appropriate next step?

<input type="radio"/>	A. Retinal transplant
<input type="radio"/>	B. Intravitreal ranibizumab
<input type="radio"/>	C. Explain no other medical therapies currently available
<input type="radio"/>	D. Photodynamic therapy
<input type="radio"/>	E. Photocoagulation

[Next question](#)

### Age related macular degeneration

Age related macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral.

Traditionally two forms of macular degeneration are seen:

- dry (geographic atrophy) macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
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- late age related macular degeneration (neovascularisation, exudative)

### Risk factors

- age: most patients are over 60 years of age
- smoking
- family history
- more common in Caucasians
- high cumulative sunlight exposure
- female sex



## Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

## Investigation and diagnosis

- optical coherence tomography: provide cross sectional views of the macula
- if neovascularisation is present fluorescein angiography is performed

## General management

- stop smoking
- high dose of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Supplements should be avoided in smokers due to an increased risk of lung cancer

## Dry macular degeneration - no current medical treatments

## Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

Which one of the following statements regarding the Holmes-Adie pupil is incorrect?

<input type="radio"/>	A. May be associated with absent ankle/knee reflexes
<input type="radio"/>	B. Bilateral in 80% of cases
<input type="radio"/>	C. It is a benign condition
<input type="radio"/>	D. Slowly reactive to accommodation but very poorly (if at all) to light
<input type="radio"/>	E. Causes a dilated pupil

Next question

The Holmes-Adie pupil is unilateral, rather than bilateral, in 80% of patients

### Holmes-Adie pupil

Holmes-Adie pupil is a benign condition most commonly seen in women. It is one of the differentials of a dilated pupil.

#### Overview

- unilateral in 80% of cases
- dilated pupil
- once the pupil has constricted it remains small for an abnormally long time
- slowly reactive to accommodation but very poorly (if at all) to light

#### Holmes-Adie syndrome

- association of Holmes-Adie pupil with absent ankle/knee reflexes

Which one of the following features is not characteristic of optic neuritis?

<input type="radio"/>	A. Eye pain worse on movement
<input type="radio"/>	B. Relative afferent pupillary defect
<input type="radio"/>	C. Poor discrimination of colours, 'red desaturation'
<input type="radio"/>	D. Sudden onset of visual loss
<input type="radio"/>	E. Central scotoma

Next question

Visual loss typically occurs over days rather than hours. Sudden visual loss due to optic neuritis is very unusual.

### Optic neuritis

#### Causes

- multiple sclerosis
- diabetes
- syphilis

#### Features

- unilateral decrease in visual acuity over hours or days
- poor discrimination of colours, 'red desaturation'
- pain worse on eye movement
- relative afferent pupillary defect
- central scotoma

#### Management

- high-dose steroids
- recovery usually takes 4-6 weeks

#### Prognosis

- MRI: if > 3 white-matter lesions, 5-year risk of developing multiple sclerosis is c. 50%

A 69-year-old man presents to the Emergency Department with blurred vision. The examining doctor suspects a diagnosis of primary open-angle glaucoma (POAG). Which one of the following features would be most consistent with a diagnosis of POAG?

<input type="radio"/>	A. Symptoms worse with mydriasis
<input type="radio"/>	B. Eye pain
<input type="radio"/>	C. Semi-dilated non-reacting pupil
<input checked="" type="radio"/>	D. Loss of nasal visual field
<input type="radio"/>	E. Red eye

[Next question](#)

The other listed symptoms are seen with acute angle closure glaucoma

### Primary open-angle glaucoma

Glaucoma is a group disorders characterised by optic neuropathy due, in the majority of patients, to raised intraocular pressure (IOP). It is now recognised that a minority of patients with raised IOP do not have glaucoma and vice versa

Primary open-angle glaucoma (POAG, also referred to as chronic simple glaucoma) is present in around 2% of people older than 40 years. Other than age, risk factors include:

- family history
- black patients
- myopia
- hypertension
- diabetes mellitus

POAG may present insidiously and for this reason is often detected during routine optometry appointments. Features may include

- peripheral visual field loss - nasal scotomas progressing to 'tunnel vision'
- decreased visual acuity
- optic disc cupping

A 74-year-old man presents with a severe throbbing headache on the right side of his head. He has now had this pain for around 6-7 days but reports no obvious trigger. There have been no visual disturbances or episodes of limb weakness. Neurological examination is unremarkable. The right side of his head is tender to touch but he cannot remember falling. Given the likely diagnosis what is the most important initial step?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Give high-dose oral prednisolone                                |
| <input type="radio"/> | B. Arrange an urgent orbital x-ray for suspected blow-out fracture |
| <input type="radio"/> | C. Arrange an urgent temporal artery biopsy                        |
| <input type="radio"/> | D. Arrange an urgent CT head                                       |
| <input type="radio"/> | E. Ocular pilocarpine + intravenous acetazolamide                  |

[Next question](#)

This patient has temporal arteritis and requires high-dose oral steroids to prevent ocular complications

### Temporal arteritis

Temporal arteritis is large vessel vasculitis which overlaps with polymyalgia rheumatica (PMR). Histology shows changes which characteristically 'skips' certain sections of affected artery whilst damaging others.

#### Features

- typically patient > 60 years old
- usually rapid onset (e.g. < 1 month)
- headache (found in 85%)
- jaw claudication (65%)
- visual disturbances secondary to anterior ischemic optic neuropathy
- tender, palpable temporal artery
- features of PMR: aching, morning stiffness in proximal limb muscles (not weakness)
- also lethargy, depression, low-grade fever, anorexia, night sweats

#### Investigations

- raised inflammatory markers: ESR > 50 mm/hr (note ESR < 30 in 10% of patients). CRP may also be elevated
- temporal artery biopsy: skip lesions may be present
- note creatine kinase and EMG normal

#### Treatment

- high-dose prednisolone - there should be a dramatic response, if not the diagnosis should be reconsidered
- urgent ophthalmology review. Patients with visual symptoms should be seen the same-day by an ophthalmologist. Visual damage is often irreversible

**Question 47 of 54**

Next

A 47-year-old female with a history of rheumatoid arthritis presents with a painful and red left eye. Visual acuity is normal. Fundoscopy is also unremarkable. What is the most likely diagnosis?

- |                       |                               |
|-----------------------|-------------------------------|
| <input type="radio"/> | A. Scleritis                  |
| <input type="radio"/> | B. Episcleritis               |
| <input type="radio"/> | C. Glaucoma                   |
| <input type="radio"/> | D. Anterior uveitis           |
| <input type="radio"/> | E. Keratoconjunctivitis sicca |

Next question

Scleritis is painful, episcleritis is not painful

A key way to discriminate between scleritis and episcleritis is the presence of pain. Keratoconjunctivitis sicca is usually bilateral and associated more with dryness, burning and itch

**Rheumatoid arthritis: ocular manifestations**

Ocular manifestations of rheumatoid arthritis are common, with 25% of patients having eye problems

**Ocular manifestations**

- keratoconjunctivitis sicca (most common)
- episcleritis (erythema)
- scleritis (erythema and pain)
- corneal ulceration
- keratitis

**Iatrogenic**

- steroid-induced cataracts
- chloroquine retinopathy

A 43-year-old who is noted to have a high-arched palate, arachnodactyly and a late-systolic murmur presents with visual problems. Which one of the following eye disorders is most associated with his underlying condition?

<input type="radio"/>	A. Superotemporal ectopia lentis
<input type="radio"/>	B. Inferonasal ectopia lentis
<input type="radio"/>	C. Retinitis pigmentosa
<input type="radio"/>	D. Acute glaucoma
<input type="radio"/>	E. Retinal detachment

[Next question](#)

This patient has features consistent with Marfan's syndrome. Whilst glaucoma and retinal detachment are seen they are not as common as superotemporal ectopia lentis (upwards lens dislocation), which is seen in around 50% of patients. Inferonasal ectopia lentis is characteristic of homocystinuria

Mitral valve prolapse may cause a late-systolic murmur. This feature helps distinguish the above description from that of a patient with homocystinuria

### Marfan's syndrome

Marfan's syndrome is an autosomal dominant connective tissue disorder. It is caused by a defect in the fibrillin-1 gene on chromosome 15 and affects around 1 in 3,000 people.

#### Features

- tall stature with arm span to height ratio  $> 1.05$
- high-arched palate
- arachnodactyly
- pectus excavatum
- pes planus
- scoliosis of  $> 20$  degrees
- heart: dilation of the aortic sinuses (seen in 90%) which may lead to aortic aneurysm, aortic dissection, aortic regurgitation, mitral valve prolapse (75%),
- lungs: repeated pneumothoraces
- eyes: upwards lens dislocation (superotemporal ectopia lentis), blue sclera, myopia
- dural ectasia (ballooning of the dural sac at the lumbosacral level)

The life expectancy of patients used to be around 40-50 years. With the advent of regular echocardiography monitoring and beta-blocker/ACE-inhibitor therapy this has improved significantly over recent years. Aortic dissection and other cardiovascular problems remain the leading cause of death however.

A 40-year-old man presents with bilateral dry, gritty eyes. A diagnosis of blepharitis is considered. Which one of the following is least likely to be associated with blepharitis?

<input type="radio"/>	A. Meibomian gland dysfunction
<input type="radio"/>	B. Seborrhoeic dermatitis
<input type="radio"/>	C. Staphylococcal infection
<input type="radio"/>	D. Acne rosacea
<input type="radio"/>	E. Viral upper respiratory tract infection

[Next question](#)

## Blepharitis

Blepharitis is inflammation of the eyelid margins. It may be due to either meibomian gland dysfunction (common, posterior blepharitis) or seborrhoeic dermatitis/staphylococcal infection (less common, anterior blepharitis). Blepharitis is also more common in patients with rosacea.

The meibomian glands secrete oil on to the eye surface to prevent rapid evaporation of the tear film. Any problem affecting the meibomian glands (as in blepharitis) can hence cause drying of the eyes which in turn leads to irritation.

### Features

- symptoms are usually bilateral
- grittiness and discomfort, particularly around the eyelid margins
- eyes may be sticky in the morning
- eyelid margins may be red. Swollen eyelids may be seen in staphylococcal blepharitis
- styes and chalazions are more common in patients with blepharitis
- secondary conjunctivitis may occur

### Management

- softening of the lid margin using hot compresses twice a day
- mechanical removal of the debris from lid margins - cotton wool buds dipped in a mixture of cooled boiled water and baby shampoo is often used\*
- artificial tears may be given for symptom relief in people with dry eyes or an abnormal tear film

\*an alternative is sodium bicarbonate, a teaspoonful in a cup of cooled water that has recently been boiled



Which one of the following best describes the action of latanoprost in the management of primary open-angle glaucoma?

- ☐ A. Carbonic anhydrase inhibitor
- ☐ B. Reduces aqueous production + increases outflow
- ☐ C. Opens up drainage pores
- ☐ D. Increases uveoscleral outflow
- ☐ E. Reduces aqueous production

[Next question](#)

### Primary open-angle glaucoma: management

The majority of patients with primary open-angle glaucoma are managed with eye drops. These aim to lower intra-ocular pressure which in turn has been shown to prevent progressive loss of visual field.

Medication	Mode of action	Notes
Prostaglandin analogues (e.g. Latanoprost)	Increases uveoscleral outflow	Once daily administration  Adverse effects include brown pigmentation of the iris
Beta-blockers (e.g. Timolol)	Reduces aqueous production	Should be avoided in asthmatics and patients with heart block
Sympathomimetics (e.g. Brimonidine, an alpha2-adrenoceptor agonist)	Reduces aqueous production and increases outflow	Avoid if taking MAOI or tricyclic antidepressants  Adverse effects include hyperaemia
Carbonic anhydrase inhibitors (e.g. Dorzolamide)	Reduces aqueous production	Systemic absorption may cause sulphonamide-like reactions
Miotics (e.g. Pilocarpine)	Increases uveoscleral outflow	Adverse effects included a constricted pupil, headache and blurred vision

Surgery in the form of a trabeculectomy may be considered in refractory cases.

A 25-year-old woman presents with a one-day history of a painful and red left eye. She describes how her eye is continually streaming tears. On examination she exhibits a degree of photophobia in the affected eye and application of fluorescein demonstrates a dendritic pattern of staining. Visual acuity is 6/6 in both eyes. What is the most appropriate management?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Topical steroid                     |
| <input type="radio"/> | B. Perform a lumbar puncture           |
| <input type="radio"/> | C. Treat with subcutaneous sumatriptan |
| <input type="radio"/> | D. Topical aciclovir                   |
| <input type="radio"/> | E. Topical chloramphenicol             |

[Next question](#)

This patient has a dendritic corneal ulcer. Topical aciclovir and ophthalmology review is required. Giving a topical steroid in this situation could be disastrous as it may worsen the infection.

### Herpes simplex keratitis

Herpes simplex keratitis most commonly presents with a dendritic corneal ulcer

#### Features

- red, painful eye
- photophobia
- epiphora
- visual acuity may be decreased
- fluorescein staining may show an epithelial ulcer

#### Management

- immediate referral to an ophthalmologist
- topical aciclovir

A 24-year-old man who has a family history of retinitis pigmentosa is reviewed in the ophthalmology clinic. He reports worsening vision over the past few months. During fundoscopy, which of the following findings with most support a diagnosis of retinitis pigmentosa?

<input type="radio"/>	A. Pigmented scrambled egg appearance concentrated around the macula
<input type="radio"/>	B. Central irregular pigmentation with bull's eye maculopathy
<input type="radio"/>	C. Black bone spicule-shaped pigmentation in the peripheral retina
<input type="radio"/>	D. Drusen with haemorrhagic atrophic changes concentrated at the periphery of the retina
<input type="radio"/>	E. Pigmented choroidal neovascularisation throughout the retina

[Next question](#)

## Retinitis pigmentosa

Retinitis pigmentosa primarily affects the peripheral retina resulting in funnel vision

### Features

- night blindness is often the initial sign
- funnel vision (the preferred term for tunnel vision)
- fundoscopy: black bone spicule-shaped pigmentation in the peripheral retina, mottling of the retinal pigment epithelium

### Associated diseases

- Refsum disease: cerebellar ataxia, peripheral neuropathy, deafness, ichthyosis
- Usher syndrome
- abetalipoproteinemia
- Lawrence-Moon-Biedl syndrome
- Kearns-Sayre syndrome
- Alport's syndrome

**Question 53 of 54**

Next

A 65-year-old man with a history of primary open-angle glaucoma presents with sudden painless loss of vision in his right eye. On examination of the right eye the optic disc is swollen with multiple flame-shaped and blot haemorrhages. What is the most likely diagnosis?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Diabetic retinopathy                |
| <input type="radio"/> | B. Vitreous haemorrhage                |
| <input type="radio"/> | C. Ischaemic optic neuropathy          |
| <input type="radio"/> | D. Occlusion of central retinal vein   |
| <input type="radio"/> | E. Occlusion of central retinal artery |

Next question

Central retinal vein occlusion - sudden painless loss of vision, severe retinal haemorrhages on fundoscopy

**Sudden painless loss of vision**

The most common causes of a sudden painless loss of vision are as follows:

- ischaemic optic neuropathy (e.g. temporal arteritis or atherosclerosis)
- occlusion of central retinal vein
- occlusion of central retinal artery
- vitreous haemorrhage
- retinal detachment

**Ischaemic optic neuropathy**

- may be due to arteritis (e.g. temporal arteritis) or atherosclerosis (e.g. hypertensive, diabetic older patient)
- due to occlusion of the short posterior ciliary arteries, causing damage to the optic nerve
- altitudinal field defects are seen

**Central retinal vein occlusion**

- incidence increases with age, more common than arterial occlusion
- causes: glaucoma, polycythaemia, hypertension
- severe retinal haemorrhages are usually seen on fundoscopy

## Central retinal artery occlusion

- due to thromboembolism (from atherosclerosis) or arteritis (e.g. temporal arteritis)
- features include afferent pupillary defect, 'cherry red' spot on a pale retina

## Vitreous haemorrhage

- causes: diabetes, bleeding disorders
- features may include sudden visual loss, dark spots

## Retinal detachment

- features of vitreous detachment, which may precede retinal detachment, include flashes of light or floaters (see below)

## Differentiating posterior vitreous detachment, retinal detachment and vitreous haemorrhage

Posterior vitreous detachment	Retinal detachment	Vitreous haemorrhage
Flashes of light (photopsia) - in the peripheral field of vision Floaters, often on the temporal side of the central vision	Dense shadow that starts peripherally progresses towards the central vision A veil or curtain over the field of vision Straight lines appear curved Central visual loss	Large bleeds cause sudden visual loss Moderate bleeds may be described as numerous dark spots Small bleeds may cause floaters

### Question 54 of 54

A 71-year-old man who has recently been diagnosed with macular degeneration asks for advice regarding antioxidant dietary supplements. Which one of the following may contraindicate the prescription of such supplements?

<input type="radio"/>	A. Current smoker
<input type="radio"/>	B. Pernicious anaemia
<input type="radio"/>	C. Treated hypertension
<input type="radio"/>	D. History of depression
<input type="radio"/>	E. Previous episodes of tendonitis

Beta-carotene has been found to increase the risk of lung cancer and hence antioxidant dietary supplements are not recommended for smokers.

### Age related macular degeneration

Age related macular degeneration is the most common cause of blindness in the UK. Degeneration of the central retina (macula) is the key feature with changes usually bilateral.

Traditionally two forms of macular degeneration are seen:

- dry (geographic atrophy) macular degeneration: characterised by drusen - yellow round spots in Bruch's membrane
- wet (exudative, neovascular) macular degeneration: characterised by choroidal neovascularisation. Leakage of serous fluid and blood can subsequently result in a rapid loss of vision. Carries worst prognosis

Recently there has been a move to a more updated classification:

- early age related macular degeneration (non-exudative, age related maculopathy): drusen and alterations to the retinal pigment epithelium (RPE)
- late age related macular degeneration (neovascularisation, exudative)

### Risk factors

- age: most patients are over 60 years of age
- smoking
- family history
- more common in Caucasians
- high cumulative sunlight exposure
- female sex

## Features

- reduced visual acuity: 'blurred', 'distorted' vision, central vision is affected first
- central scotomas
- fundoscopy: drusen, pigmentary changes

## Investigation and diagnosis

- optical coherence tomography: provide cross sectional views of the macula
- if neovascularisation is present fluorescein angiography is performed

## General management

- stop smoking
- high dose of beta-carotene, vitamins C and E, and zinc may help to slow down visual loss for patients with established macular degeneration. Supplements should be avoided in smokers due to an increased risk of lung cancer

## Dry macular degeneration - no current medical treatments

## Wet macular degeneration

- photocoagulation
- photodynamic therapy
- anti-vascular endothelial growth factor (anti-VEGF) treatments: intravitreal ranibizumab

**Question 1 of 56**

Next

A 54-year-old man presents with a variety of physical symptoms that have been present for the past 9 years. Numerous investigations and review by a variety of specialties have indicated no organic basis for his symptoms. This is an example of:

<input type="radio"/>	A. Munchausen's syndrome
<input type="radio"/>	B. Hypochondrial disorder
<input type="radio"/>	C. Dissociative disorder
<input checked="" type="radio"/>	D. Somatisation disorder
<input type="radio"/>	E. Conversion disorder

Next question

**Unexplained symptoms**

- Somatisation = Symptoms
- hypoChondria = Cancer

Somatisation disorder is the correct answer as the patient is concerned about persistent, unexplained symptoms rather than an underlying diagnosis such as cancer (hypochondrial disorder). Munchausen's syndrome describes the intentional production of symptoms, for example self poisoning

**Unexplained symptoms**

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

**Somatisation disorder**

- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

**Hypochondrial disorder**

- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

**Conversion disorder**

- typically involves loss of motor or sensory function



- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

#### Dissociative disorder

- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

#### Munchausen's syndrome

- also known as factitious disorder
- the intentional production of physical or psychological symptoms

#### Malingering

- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

## Question 2 of 56

Next

Which one of the following is **not** a recognised feature of anorexia nervosa?

<input type="radio"/>	A. Hypokalaemia
<input type="radio"/>	B. Low LH
<input type="radio"/>	C. Impaired glucose tolerance
<input type="radio"/>	D. Low FSH
<input type="radio"/>	E. Reduced growth hormone levels

Next question

### Anorexia features

- most things low
- **G's and C's raised: growth hormone, glucose, salivary glands, cortisol, cholesterol, carotinaemia**

### Anorexia nervosa: features

Anorexia nervosa is associated with a number of characteristic clinical signs and physiological abnormalities which are summarised below

#### Features

- reduced body mass index
- bradycardia
- hypotension
- enlarged salivary glands

#### Physiological abnormalities

- hypokalaemia
- low FSH, LH, oestrogens and testosterone
- raised cortisol and growth hormone
- impaired glucose tolerance
- hypercholesterolaemia
- hypercarotinaemia
- low T3

### Question 3 of 56

Next

Which one of the following symptoms may indicate mania rather than hypomania?

<input type="radio"/>	A. Predominately elevated mood
<input type="radio"/>	B. Delusions of grandeur
<input type="radio"/>	C. Increased appetite
<input type="radio"/>	D. Flight of ideas
<input type="radio"/>	E. Irritability

Next question

### Hypomania vs. mania

The presence of psychotic symptoms differentiates mania from hypomania

Psychotic symptoms

- delusions of grandeur
- auditory hallucinations

The following symptoms are common to both hypomania and mania

Mood

- predominately elevated
- irritable

Speech and thought

- pressured
- flight of ideas
- poor attention

Behaviour

- insomnia
- loss of inhibitions: sexual promiscuity, overspending, risk-taking
- increased appetite

#### Question 4 of 56

Next

A 45-year-old man who takes chlorpromazine for schizophrenia presents with severe restlessness. What side-effect of antipsychotic medication is this an example of?

<input type="radio"/>	A. Akathisia
<input type="radio"/>	B. Neuroleptic malignant syndrome
<input type="radio"/>	C. Acute dystonia
<input type="radio"/>	D. Tardive dyskinesia
<input type="radio"/>	E. Parkinsonism

Next question

### Antipsychotics

Antipsychotics act as dopamine D2 receptor antagonists, blocking dopaminergic transmission in the mesolimbic pathways. Conventional antipsychotics are associated with problematic extrapyramidal side-effects which has led to the development of atypical antipsychotics such as clozapine

#### Extrapyramidal side-effects

- Parkinsonism
- acute dystonia (e.g. torticollis, oculogyric crisis)
- akathisia (severe restlessness)
- tardive dyskinesia (late onset of choreoathetoid movements, abnormal, involuntary, may occur in 40% of patients, may be irreversible, most common is chewing and pouting of jaw)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:

- increased risk of stroke
- increased risk of venous thromboembolism

#### Other side-effects

- antimuscarinic: dry mouth, blurred vision, urinary retention, constipation
- sedation, weight gain
- raised prolactin: galactorrhoea
- neuroleptic malignant syndrome: pyrexia, muscle stiffness
- reduced seizure threshold (greater with atypicals)

### Question 5 of 56

Next

A 25-year-old man demands a CT scan of his abdomen in clinic. He states it is 'obvious' he has cancer despite previous negative investigations. This is an example of a:

<input type="radio"/>	A. Hypochondrial disorder
<input type="radio"/>	B. Conversion disorder
<input type="radio"/>	C. Munchausen's syndrome
<input type="radio"/>	D. Dissociative disorder
<input type="radio"/>	E. Somatisation disorder

Next question

#### Unexplained symptoms

- Somatisation = Symptoms
- hypoChondria = Cancer

### Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

#### Somatisation disorder

- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

#### Hypochondrial disorder

- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

#### Conversion disorder

- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

## Dissociative disorder

- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

## Munchausen's syndrome

- also known as factitious disorder
- the intentional production of physical or psychological symptoms

## Malingering

- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

## Question 6 of 56

Next

A 34-year-old man confides in you that he experienced childhood sexual abuse. Which one of the following features is not a characteristic feature of post-traumatic stress disorder?

<input type="radio"/>	A. Hyperarousal
<input type="radio"/>	B. Emotional numbing
<input type="radio"/>	C. Nightmares
<input type="radio"/>	D. Loss of inhibitions
<input type="radio"/>	E. Avoidance

Next question

### Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) can develop in people of any age following a traumatic event, for example a major disaster or childhood sexual abuse. It encompasses what became known as 'shell shock' following the first world war. One of the DSM-IV diagnostic criteria is that symptoms have been present for more than one month

#### Features

- re-experiencing: flashbacks, nightmares, repetitive and distressing intrusive images
- avoidance: avoiding people, situations or circumstances resembling or associated with the event
- hyperarousal: hypervigilance for threat, exaggerated startle response, sleep problems, irritability and difficulty concentrating
- emotional numbing - lack of ability to experience feelings, feeling detached

from other people

- depression
- drug or alcohol misuse
- anger
- unexplained physical symptoms

#### Management

- following a traumatic event single-session interventions (often referred to as debriefing) are not recommended
- watchful waiting may be used for mild symptoms lasting less than 4 weeks
- military personnel have access to treatment provided by the armed forces
- trauma-focused cognitive behavioural therapy (CBT) or eye movement desensitisation and reprocessing (EMDR) therapy may be used in more severe cases
- drug treatments for PTSD should not be used as a routine first-line treatment for adults. If drug treatment is used then paroxetine or mirtazapine are recommended

A 25-year-old man with a history of schizophrenia is prescribed olanzapine. Which one of the following adverse effects is he most likely to experience?

<input type="radio"/>	A. Anorexia
<input type="radio"/>	B. Parkinsonism
<input type="radio"/>	C. Hypertension
<input type="radio"/>	D. Weight gain
<input type="radio"/>	E. Agranulocytosis

Weight gain is an extremely common adverse effect of atypical antipsychotics such as olanzapine

### Atypical antipsychotics

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics

- weight gain
- clozapine is associated with agranulocytosis (see below)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:

- increased risk of stroke (especially olanzapine and risperidone)
- increased risk of venous thromboembolism

Examples of atypical antipsychotics

- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride

Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in patients resistant to other antipsychotic medication

Adverse effects of clozapine

- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients



A 39-year-old man comes for review. Six months ago he was started on paroxetine for depression. Around five days ago he stopped taking the medication as he felt that it was having no benefit. His only past medical history of note is asthma. For the past two days he has experienced increased anxiety, sweating, headache and the feeling of a needle like sensation in his head. During the consultation he is pacing around the room. What is the most explanation for his symptoms?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. Bipolar disorder  |
| <input type="radio"/> | B. Malingering   |
| <input type="radio"/> | C. Selective serotonin reuptake inhibitor discontinuation syndrome |
| <input type="radio"/> | D. Migraine  |
| <input type="radio"/> | E. Generalised anxiety disorder                                    |

[Next question](#)

Paroxetine has a higher incidence of discontinuation symptoms than other selective serotonin reuptake inhibitors.

### Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are considered first-line treatment for the majority of patients with depression.

- citalopram and fluoxetine are currently the preferred SSRIs
- citalopram is useful for elderly patients as it is associated with lower risks of drug interactions
- sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants
- SSRIs should be used with caution in children and adolescents. Fluoxetine is the drug of choice when an antidepressant is indicated

### Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline are more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

## Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', but if given co-prescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

## Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paraesthesia

**Question 9 of 56**

Next

You are considering prescribing a tricyclic antidepressant for a patient who has not responded to two different types of selective serotonin reuptake inhibitors. Which one of the following tricyclic antidepressants is most dangerous in overdose?

- |                       |                  |
|-----------------------|------------------|
| <input type="radio"/> | A. Dosulepin     |
| <input type="radio"/> | B. Imipramine    |
| <input type="radio"/> | C. Clomipramine  |
| <input type="radio"/> | D. Nortriptyline |
| <input type="radio"/> | E. Lofepramine   |

Next question

Dosulepin - avoid as dangerous in overdose

**Tricyclic antidepressants**

Tricyclic antidepressants (TCAs) are used less commonly now for depression due to their side-effects and toxicity in overdose. They are however used widely in the treatment of neuropathic pain, where smaller doses are typically required.

**Common side-effects**

- drowsiness
- dry mouth
- blurred vision
- constipation
- urinary retention

**Choice of tricyclic**

- low-dose amitriptyline is commonly used in the management of neuropathic pain and the prophylaxis of headache (both tension and migraine)
- lofepramine has a lower incidence of toxicity in overdose
- amitriptyline and dosulepin (dothiepin) are considered the most dangerous in overdose

More sedative	Less sedative
Amitriptyline	Imipramine
Clomipramine	Lofepramine
Dosulepin	Nortriptyline
Trazodone*	

\*trazodone is technically a 'tricyclic-related antidepressant'

**Question 10 of 56**

Next

A 23-year-old male presents to his GP two weeks after a road traffic accident concerned about increased anxiety levels, lethargy and headache. At the time he had a CT brain after banging his head on the steering wheel, which revealed no abnormality. Six months following this episode his symptoms have resolved. What did his original symptoms likely represent?

- |                       |                                   |
|-----------------------|-----------------------------------|
| <input type="radio"/> | A. Conversion disorder            |
| <input type="radio"/> | B. Post-traumatic stress disorder |
| <input type="radio"/> | C. Somatisation disorder          |
| <input type="radio"/> | D. Generalised anxiety disorder   |
| <input type="radio"/> | E. Post-concussion syndrome       |

Next question

In post-traumatic stress disorder the onset of symptoms is usually delayed and it tends to run a prolonged course

**Post-concussion syndrome**

Post-concussion syndrome is seen after even minor head trauma

Typical features include

- headache
- fatigue
- anxiety/depression
- dizziness

An elderly patient in a nursing home is started on quetiapine due to persistent aggressive behaviour that has not responded to non-pharmacological approaches. Which of the following adverse effects do antipsychotics increase the risk of in elderly patients?

<input type="radio"/>	A. Atrial fibrillation
<input type="radio"/>	B. Myocardial infarction
<input type="radio"/>	C. Aspiration pneumonia
<input type="radio"/>	D. Stroke
<input type="radio"/>	E. Breast cancer

Antipsychotics in the elderly - increased risk of stroke and VTE

## Antipsychotics

Antipsychotics act as dopamine D2 receptor antagonists, blocking dopaminergic transmission in the mesolimbic pathways. Conventional antipsychotics are associated with problematic extrapyramidal side-effects which has led to the development of atypical antipsychotics such as clozapine

### Extrapyramidal side-effects

- Parkinsonism
- acute dystonia (e.g. torticollis, oculogyric crisis)
- akathisia (severe restlessness)
- tardive dyskinesia (late onset of choreoathetoid movements, abnormal, involuntary, may occur in 40% of patients, may be irreversible, most common is chewing and pouting of jaw)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:

- increased risk of stroke
- increased risk of venous thromboembolism

### Other side-effects

- antimuscarinic: dry mouth, blurred vision, urinary retention, constipation
- sedation, weight gain
- raised prolactin: galactorrhoea
- neuroleptic malignant syndrome: pyrexia, muscle stiffness
- reduced seizure threshold (greater with atypicals)

A 30-year-old man presents to his doctor as he has been feeling generally 'out of sorts' for the past few weeks. He is accompanied by his girlfriend who says he has 'not been himself'. She is worried and feels he may need to see a psychiatrist. There is no history of past mental health problems. Which one of the following symptoms would be most suggestive of depression?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Palpitations   |
| <input type="radio"/> | B. Nausea before certain situations e.g. getting on a bus |
| <input type="radio"/> | C. Early morning waking                                   |
| <input type="radio"/> | D. Excessive gambling                                     |
| <input type="radio"/> | E. Flash-backs to childhood problems                      |

[Next question](#)

Early morning waking is a classic somatic symptom of depression and often develops earlier than general insomnia.

Palpitations and nausea are more common with anxiety. Excessive gambling may suggest either a simple gambling addiction or be part of a hypomanic/manic disorder.

Flash-backs are common in post-traumatic stress disorder.

## Depression: screening and assessment

### Screening

The following two questions can be used to screen for depression

- 'During the last month, have you often been bothered by feeling down, depressed or hopeless?'
- 'During the last month, have you often been bothered by having little interest or pleasure in doing things?'

A 'yes' answer to either of the above should prompt a more in depth assessment.

### Assessment

There are many tools to assess the degree of depression including the Hospital Anxiety and Depression (HAD) scale and the Patient Health Questionnaire (PHQ-9).

Hospital Anxiety and Depression (HAD) scale

- consists of 14 questions, 7 for anxiety and 7 for depression
- each item is scored from 0-3
- produces a score out of 21 for both anxiety and depression
- severity: 0-7 normal, 8-10 borderline, 11+ case

- patients should be encouraged to answer the questions quickly

### Patient Health Questionnaire (PHQ-9)

- asks patients 'over the last 2 weeks, how often have you been bothered by any of the following problems?'
- 9 items which can then be scored 0-3
- includes items asking about thoughts of self-harm
- depression severity: 0-4 none, 5-9 mild, 10-14 moderate, 15-19 moderately severe, 20-27 severe

**NICE** use the **DSM-IV** criteria to grade depression:

- 1. Depressed mood most of the day, nearly every day
- 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
- 3. Significant weight loss or weight gain when not dieting or decrease or increase in appetite nearly every day
- 4. Insomnia or hypersomnia nearly every day
- 5. Psychomotor agitation or retardation nearly every day
- 6. Fatigue or loss of energy nearly every day
- 7. Feelings of worthlessness or excessive or inappropriate guilt nearly every day
- 8. Diminished ability to think or concentrate, or indecisiveness nearly every day
- 9. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

<b>Subthreshold depressive symptoms</b>	Fewer than 5 symptoms
<b>Mild depression</b>	Few, if any, symptoms in excess of the 5 required to make the diagnosis, and symptoms result in only minor functional impairment
<b>Moderate depression</b>	Symptoms or functional impairment are between 'mild' and 'severe'
<b>Severe depression</b>	Most symptoms, and the symptoms markedly interfere with functioning. Can occur with or without psychotic symptoms

A 23-year-old man asks to be referred to a plastic surgeon. From his records you can see he has been treated for anxiety and depression with fluoxetine previously and has been off work with back pain for the past three months. He is concerned that his ears are too big in proportion to his face. He reports that he now seldom leaves the house because of this. On examination his ears appear to be within normal limits. What is the most appropriate description of this behaviour?

<input type="radio"/>	A. Hypochondriasis
<input type="radio"/>	B. Generalised anxiety disorder
<input type="radio"/>	C. Somatisation
<input type="radio"/>	D. Malingering
<input type="radio"/>	E. Dysmorphophobia

[Next question](#)

### Body dysmorphic disorder

Body dysmorphic disorder (sometimes referred to as dysmorphophobia) is a mental disorder where patients have a significantly distorted body image

Diagnostic and Statistical Manual (DSM) IV criteria:

- Preoccupation with an imagined defect in appearance. If a slight physical anomaly is present, the person's concern is markedly excessive
- The preoccupation causes clinically significant distress or impairment in social, occupational, or other important areas of functioning
- The preoccupation is not better accounted for by another mental disorder (e.g., dissatisfaction with body shape and size in Anorexia Nervosa)



### Question 14 of 56

Next

A 68-year-old female is noted to be depressed following a recent admission for an exacerbation of chronic obstructive pulmonary disease. What would be the most appropriate antidepressant to start?

<input type="radio"/>	A. Fluoxetine
<input type="radio"/>	B. Citalopram
<input type="radio"/>	C. Venlafaxine
<input type="radio"/>	D. Paroxetine
<input type="radio"/>	E. Imipramine

Next question

Citalopram and fluoxetine are currently the preferred SSRIs. Citalopram is more appropriate in this scenario as it has a lower propensity for drug interactions.

#### Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are considered first-line treatment for the majority of patients with depression.

- citalopram and fluoxetine are currently the preferred SSRIs
- citalopram is useful for elderly patients as it is associated with lower risks of drug interactions
- sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants
- SSRIs should be used with caution in children and adolescents. Fluoxetine is the drug of choice when an antidepressant is indicated

#### Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline are more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

#### Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', but if given co-prescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above

- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

#### Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paraesthesia

A woman who gave birth 5 days ago presents for review as she is concerned about her mood. She is having difficulty sleeping and feels generally anxious and tearful. Since giving birth she has also found herself snapping at her husband. This is her first pregnancy, she is not breast feeding and there is no history of mental health disorders in the past. What is the most appropriate management?

- ☐ A. Explanation and reassurance
- ☐ B. Cognitive behavioural therapy
- ☐ C. Trial of fluoxetine
- ☐ D. Trial of citalopram
- ☐ E. Discuss with psychiatric team to consider admission to mother and baby unit

Next question

This woman has the baby-blues which is seen in around two-thirds of women. Whilst poor sleeping can be a sign of depression it is to be expected with a new baby!

### Post-partum mental health problems

Post-partum mental health problems range from the 'baby-blues' to puerperal psychosis

'Baby-blues'	Postnatal depression	Puerperal psychosis
Seen in around 60-70% of women	Affects around 10% of women	Affects approximately 0.2% of women
Typically seen 3-7 days following birth and is more common in primips	Most cases start within a month and typically peaks at 3 months	Onset usually within the first 2-3 weeks following birth
Mothers are characteristically anxious, tearful and irritable	Features are similar to depression seen in other circumstances	Features include severe swings in mood (similar to bipolar disorder) and disordered perception (e.g. auditory hallucinations)
Reassurance and support, the health visitor has a key role	As with the baby blues reassurance and support are important  Cognitive behavioural therapy may be beneficial. Certain SSRIs such as sertraline and paroxetine* may be used if symptoms are severe** - whilst they are secreted in breast milk it is not thought to be harmful to the infant	Admission to hospital is usually required  There is around a 20% risk of recurrence following future pregnancies

\*paroxetine is recommended by SIGN because of the low milk/plasma ratio

\*\*fluoxetine is best avoided due to a long half-life

A 18-year-old sprinter who is currently preparing for a national athletics meeting asks to see the team doctor due to an unusual sensation in his legs. He describes a numb sensation below his knee. On examination the patient there is apparent sensory loss below the right knee in a non-dermatomal distribution. The team doctor suspects a non-organic cause of his symptoms. This is an example of a:

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Conversion disorder    |
| <input type="radio"/> | B. Hypochondrial disorder |
| <input type="radio"/> | C. Somatisation disorder  |
| <input type="radio"/> | D. Malingering            |
| <input type="radio"/> | E. Munchausen's syndrome  |

[Next question](#)

## Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

### Somatisation disorder

- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

### Hypochondrial disorder

- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

### Conversion disorder

- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

### Dissociative disorder

- dissociation is a process of 'separating off' certain memories from normal consciousness

- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

#### Munchausen's syndrome

- also known as factitious disorder
- the intentional production of physical or psychological symptoms

#### Malingering

- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

A 23-year-old man presents as he is concerned about a number of recent episodes related to sleep. He finds when he wakes up and less often when he is falling asleep he is 'paralysed' and unable to move. This sometimes associated with what the patient describes as 'hallucinations' such as seeing another person in the room. He is becoming increasingly anxious about these recent episodes. What is the most likely diagnosis?

- |                       |                                 |
|-----------------------|---------------------------------|
| <input type="radio"/> | A. Frontal lobe epilepsy        |
| <input type="radio"/> | B. Generalised anxiety disorder |
| <input type="radio"/> | C. Sleep paralysis              |
| <input type="radio"/> | D. Night terrors                |
| <input type="radio"/> | E. Acute schizophrenia          |

[Next question](#)

## Sleep paralysis

Sleep paralysis is a common condition characterized by transient paralysis of skeletal muscles which occurs when awakening from sleep or less often while falling asleep. It is thought to be related to the paralysis that occurs as a natural part of REM (rapid eye movement) sleep. Sleep paralysis is recognised in a wide variety of cultures

### Features

- paralysis - this occurs after waking up or shortly before falling asleep
- hallucinations - images or speaking that appear during the paralysis

### Management

- if troublesome clonazepam may be used

**Question 18 of 56**

Next

A 34-year-old man originally from West Africa is seen in January with depression. There is no past medical history of note but he is known to smoke cannabis. He has had similar episodes for the past two winters. What is the most likely diagnosis?

- |                       |                                |
|-----------------------|--------------------------------|
| <input type="radio"/> | A. Cyclothymic disorder        |
| <input type="radio"/> | B. Atypical depression         |
| <input type="radio"/> | C. Seasonal affective disorder |
| <input type="radio"/> | D. Schizophrenia               |
| <input type="radio"/> | E. Drug-induced depression     |

Next question

**Seasonal affective disorder**

Seasonal affective disorder (SAD) describes depression which occurs predominately around the winter months. Bright light therapy has been shown to be more effective than placebo for patients with SAD

You review a patient who has been taking citalopram for the past two years to treat depression. He has felt well now for the past year and you agree a plan to stop the antidepressant. How should the citalopram be stopped?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Can be stopped immediately               |
| <input type="radio"/> | B. Withdraw gradually over the next 3 days  |
| <input type="radio"/> | C. Withdraw gradually over the next week    |
| <input type="radio"/> | D. Withdraw gradually over the next 2 weeks |
| <input type="radio"/> | E. Withdraw gradually over the next 4 weeks |

[Next question](#)

This not necessary with fluoxetine due to its longer half-life.

### Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are considered first-line treatment for the majority of patients with depression.

- citalopram and fluoxetine are currently the preferred SSRIs
- citalopram is useful for elderly patients as it is associated with lower risks of drug interactions
- sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants
- SSRIs should be used with caution in children and adolescents. Fluoxetine is the drug of choice when an antidepressant is indicated

### Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline are more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

### Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', but if given co-prescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs



Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

#### Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paraesthesia

Which one of the following side-effects is more common with atypical than conventional anti-psychotics?

<input type="radio"/>	A. Akathisia
<input type="radio"/>	B. Weight gain
<input type="radio"/>	C. Galactorrhoea
<input type="radio"/>	D. Parkinsonism
<input type="radio"/>	E. Tardive dyskinesia

Next question

Atypical antipsychotics commonly cause weight gain

### Atypical antipsychotics

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics

- weight gain
- clozapine is associated with agranulocytosis (see below)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:

- increased risk of stroke (especially olanzapine and risperidone)
- increased risk of venous thromboembolism

Examples of atypical antipsychotics

- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride

Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full

blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in patients resistant to other antipsychotic medication

#### Adverse effects of clozapine

- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients

**Question 21 of 56**

Next

A 45-year-old man is admitted due to haematemesis. He drinks 120 units of alcohol a week. When is the peak incidence of seizures following alcohol withdrawal?

- |                       |             |
|-----------------------|-------------|
| <input type="radio"/> | A. 2 hours  |
| <input type="radio"/> | B. 6 hours  |
| <input type="radio"/> | C. 12 hours |
| <input type="radio"/> | D. 24 hours |
| <input type="radio"/> | E. 36 hours |

Next question

**Alcohol withdrawal**

- symptoms: 6-12 hours
- seizures: 36 hours
- delirium tremens: 72 hours

**Alcohol withdrawal****Mechanism**

- chronic alcohol consumption enhances GABA mediated inhibition in the CNS (similar to benzodiazepines) and inhibits NMDA-type glutamate receptors
- alcohol withdrawal is thought to lead to the opposite (decreased inhibitory GABA and increased NMDA glutamate transmission)

**Features**

- symptoms start at 6-12 hours
- peak incidence of seizures at 36 hours
- peak incidence of delirium tremens is at 72 hours

**Management**

- benzodiazepines
- carbamazepine also effective in treatment of alcohol withdrawal
- phenytoin is said not to be as effective in the treatment of alcohol withdrawal seizures

**Question 22 of 56**

Next

Which of the following conditions is least associated with obsessive compulsive disorder?

<input type="radio"/>	A. Tourette's syndrome
<input type="radio"/>	B. Anorexia nervosa
<input type="radio"/>	C. Schizophrenia
<input type="radio"/>	D. Depression
<input type="radio"/>	E. Wilson's disease

Next question

**OCD**

## Pathophysiology

- some research suggest childhood group A beta-haemolytic streptococcal infection may have a role

## Associations

- depression (30%)
- schizophrenia (3%)
- Sydenham's chorea
- Tourette's syndrome
- anorexia nervosa

A 54-year-old man with a history of depression presents for review. He was started on fluoxetine eight weeks ago and is now requesting to stop his medication as he feels so well. What should be recommended regarding his treatment?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. It should be stopped straight away                    |
| <input type="radio"/> | B. It should be continued for at least another 6 weeks   |
| <input type="radio"/> | C. It should be continued for at least another 3 months  |
| <input type="radio"/> | D. It should be continued for at least another 6 months  |
| <input type="radio"/> | E. It should be continued for at least another 12 months |

[Next question](#)

This greatly reduces the risk of relapse. Patients should be reassured that antidepressants are not addictive.

### Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are considered first-line treatment for the majority of patients with depression.

- citalopram and fluoxetine are currently the preferred SSRIs
- citalopram is useful for elderly patients as it is associated with lower risks of drug interactions
- sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants
- SSRIs should be used with caution in children and adolescents. Fluoxetine is the drug of choice when an antidepressant is indicated

### Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline are more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

### Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', but if given co-prescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above

- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

#### Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paraesthesia

Which one of the following is not associated with a poor prognosis in schizophrenia?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Acute onset                            |
| <input type="radio"/> | B. Strong family history                  |
| <input type="radio"/> | C. Low IQ                                 |
| <input type="radio"/> | D. Premorbid history of social withdrawal |
| <input type="radio"/> | E. Lack of obvious precipitant            |

Next question

A gradual, rather than acute, onset is associated with a poor prognosis

### Schizophrenia: prognostic indicators

Factors associated with poor prognosis

- strong family history
- gradual onset
- low IQ
- premorbid history of social withdrawal
- lack of obvious precipitant



**Question 25 of 56**[Next](#)

A 24-year-old female is reviewed following a course of cognitive behaviour therapy for bulimia. She feels there has been no improvement in her condition and is interested in trying pharmacological treatments. Which one of the following is most suitable?

<input type="radio"/>	A. Low-dose citalopram
<input type="radio"/>	B. Low-dose fluoxetine
<input type="radio"/>	C. Low-dose amitriptyline
<input type="radio"/>	D. High-dose amitriptyline
<input type="radio"/>	E. High-dose fluoxetine

[Next question](#)**Bulimia nervosa**

Bulimia nervosa is a type of eating disorder characterised by episodes of binge eating followed by intentional vomiting

**Management**

- referral for specialist care is appropriate in all cases
- cognitive behaviour therapy (CBT) is currently consider first-line treatment
- interpersonal psychotherapy is also used but takes much longer than CBT
- pharmacological treatments have a limited role - a trial of high-dose fluoxetine is currently licensed for bulimia but long-term data is lacking

Which one of the following statements regarding anorexia nervosa is correct?

- |                       |  |
|-----------------------|--|
| <input type="radio"/> | A. The BMI should be $< 16.5 \text{ kg/m}^2$ before making the diagnosis               |
| <input type="radio"/> | B. If amenorrhoea is present a hormonal disorder needs to be excluded                  |
| <input type="radio"/> | C. It is the most common cause of admissions to child and adolescent psychiatric wards |
| <input type="radio"/> | D. Around 75-80% of the patients are female  |
| <input type="radio"/> | E. Has a good prognosis if treated   |

Next question

## Anorexia nervosa

Anorexia nervosa is the most common cause of admissions to child and adolescent psychiatric wards.

### Epidemiology

- 90% of patients are female
- predominately affects teenage and young-adult females
- prevalence of between 1:100 and 1:200

### Diagnosis (based on the DSM-IV criteria)

- person chooses not to eat - BMI  $< 17.5 \text{ kg/m}^2$ , or  $< 85\%$  of that expected
- intense fear of being obese
- disturbance of weight perception
- amenorrhoea = 3 consecutive cycles

The prognosis of patients with anorexia nervosa remains poor. Up to 10% of patients will eventually die because of the disorder.

A 24-year-old male is admitted to the Emergency Department complaining of severe abdominal pain. On examination he is shivering and rolling around the trolley. He has previously been investigated for abdominal pain and no cause has been found. He states that unless he is given morphine for the pain he will kill himself. This is an example of:

- |                       |                           |
|-----------------------|---------------------------|
| <input type="radio"/> | A. Hypochondrial disorder |
| <input type="radio"/> | B. Conversion disorder    |
| <input type="radio"/> | C. Malingering            |
| <input type="radio"/> | D. Munchausen's syndrome  |
| <input type="radio"/> | E. Somatisation disorder  |

[Next question](#)

This is difficult as the patient may well be an opiate abuser who is withdrawing. However, given the above options the most appropriate term to use is malingering as the patient is reporting symptoms with the deliberate intention of getting morphine

### Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

#### Somatisation disorder

- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

#### Hypochondrial disorder

- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

#### Conversion disorder

- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

#### Dissociative disorder

- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

#### Munchausen's syndrome

- also known as factitious disorder
- the intentional production of physical or psychological symptoms

#### Malingering

- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

**Question 28 of 56**

Next

A 14-year-old boy is brought for review. He is normally fit and well and hasn't seen a doctor for over five years. His mother has been increasingly concerned about his behaviour in the past few weeks. She describes him staying up late at night, talking quickly and being very irritable. Yesterday he told his mother he was planning to 'take-over' the school assembly and give 'constructive criticism' to his teachers in front of the other pupils. He feels many of his teachers are 'underperforming' and need to be 'retaught' their subjects by him. He admits to trying cannabis once around six months ago and has drunk alcohol 'a few times' in the past year, the last time being two weeks ago. Prior to his deterioration a few weeks ago his mother describes him as a happy, well-adjusted, sociable young man. Which one of the following is the most likely diagnosis?

<input type="radio"/>	A. Hypomania
<input type="radio"/>	B. Cannabis-induced psychosis
<input type="radio"/>	C. Mania
<input type="radio"/>	D. Alcoholic hallucinosis
<input type="radio"/>	E. Asperger's syndrome

Next question

Cannabis and alcohol related problems are very unlikely given how long ago he used those substances. The delusions of grandeur imply this is mania rather than hypomania.

**Hypomania vs. mania**

The presence of psychotic symptoms differentiates mania from hypomania

Psychotic symptoms

- delusions of grandeur
- auditory hallucinations

The following symptoms are common to both hypomania and mania

Mood

- predominately elevated
- irritable

Speech and thought

- pressured
- flight of ideas
- poor attention

## Behaviour

- insomnia
- loss of inhibitions: sexual promiscuity, overspending, risk-taking
- increased appetite

**Question 29 of 56**

Next

A 27-year-old woman is brought in by her husband. She has been refusing to go outside for the past 3 months, telling her husband she is afraid of catching avian flu. On exploring this further she is concerned due to the high number of migrating birds she can see in her garden. She reports that the presence of her husbands socks on the washing line in the garden alerted her to this. What is the most likely diagnosis?

- |                       |                                    |
|-----------------------|------------------------------------|
| <input type="radio"/> | A. Depression                      |
| <input type="radio"/> | B. Hypochondrial disorder          |
| <input type="radio"/> | C. Formal thought disorder         |
| <input type="radio"/> | D. Borderline personality disorder |
| <input type="radio"/> | E. Acute paranoid schizophrenia    |

Next question

The washing line comment is an example of a delusional perception - see below

**Schizophrenia: features**

Schneider's first rank symptoms may be divided into auditory hallucinations, thought disorders, passivity phenomena and delusional perceptions:

Auditory hallucinations of a specific type:

- two or more voices discussing the patient in the third person
- thought echo
- voices commenting on the patient's behaviour

Thought disorder\*:

- thought insertion
- thought withdrawal
- thought broadcasting

Passivity phenomena:

- bodily sensations being controlled by external influence
- actions/impulses/feelings - experiences which are imposed on the individual or influenced by others

Delusional perceptions

- a two stage process) where first a normal object is perceived then secondly there is a sudden intense delusional insight into the objects meaning for the patient e.g. 'The traffic light is green therefore I am the King'.

Other features of schizophrenia include

- impaired insight
- incongruity/blunting of affect (inappropriate emotion for circumstances)
- decreased speech
- neologisms: made-up words
- catatonia
- negative symptoms: incongruity/blunting of affect, anhedonia (inability to derive pleasure), alogia (poverty of speech), avolition (poor motivation)

\*occasionally referred to as thought alienation



A 29-year-old fireman presents following a recent traumatic incident where a child died in a house fire. He describes recurrent nightmares and flashbacks which have been present for the past 3 months. A diagnosis of post-traumatic stress disorder is suspected. What is the most appropriate first-line treatment?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Arrange a CT head to exclude an organic cause  |
| <input type="radio"/> | B. Cognitive behavioural therapy or eye movement desensitisation and reprocessing therapy |
| <input type="radio"/> | C. Cognitive behavioural therapy or graded exposure therapy                               |
| <input type="radio"/> | D. Cognitive behavioural therapy or psychodynamic therapy                                 |
| <input type="radio"/> | E. Watchful waiting   |

[Next question](#)

### Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) can develop in people of any age following a traumatic event, for example a major disaster or childhood sexual abuse. It encompasses what became known as 'shell shock' following the first world war. One of the DSM-IV diagnostic criteria is that symptoms have been present for more than one month

#### Features

- re-experiencing: flashbacks, nightmares, repetitive and distressing intrusive images
- avoidance: avoiding people, situations or circumstances resembling or associated with the event
- hyperarousal: hypervigilance for threat, exaggerated startle response, sleep problems, irritability and difficulty concentrating
- emotional numbing - lack of ability to experience feelings, feeling detached

#### from other people

- depression
- drug or alcohol misuse
- anger
- unexplained physical symptoms

#### Management

- following a traumatic event single-session interventions (often referred to as debriefing) are not recommended
- watchful waiting may be used for mild symptoms lasting less than 4 weeks
- military personnel have access to treatment provided by the armed forces
- trauma-focused cognitive behavioural therapy (CBT) or eye movement desensitisation and reprocessing (EMDR) therapy may be used in more severe cases
- drug treatments for PTSD should not be used as a routine first-line treatment for adults. If drug treatment is used then paroxetine or mirtazapine are recommended

A patient you are looking after is started on imipramine for depression. Which combination of side-effects is most likely to be seen in a patient taking this class of antidepressants?

<input type="radio"/>	A. Dry mouth + urinary frequency
<input type="radio"/>	B. Hypertension + sweating
<input type="radio"/>	C. Gastrointestinal bleeding + dyspepsia
<input type="radio"/>	D. Headache + myoclonus
<input type="radio"/>	E. Blurred vision + dry mouth

[Next question](#)

These antimuscarinic side-effects are more common with imipramine than other types of tricyclic antidepressants.

### Tricyclic antidepressants

Tricyclic antidepressants (TCAs) are used less commonly now for depression due to their side-effects and toxicity in overdose. They are however used widely in the treatment of neuropathic pain, where smaller doses are typically required.

#### Common side-effects

- drowsiness
- dry mouth
- blurred vision
- constipation
- urinary retention

#### Choice of tricyclic

- low-dose amitriptyline is commonly used in the management of neuropathic pain and the prophylaxis of headache (both tension and migraine)
- lofepramine has a lower incidence of toxicity in overdose
- amitriptyline and dosulepin (dothiepin) are considered the most dangerous in overdose

More sedative	Less sedative
Amitriptyline	Imipramine
Clomipramine	Lofepramine
Dosulepin	Nortriptyline
Trazodone*	

\*trazodone is technically a 'tricyclic-related antidepressant'

Which one of the following statements regarding post-partum mental health problems is NOT true?

- ☐ A. Post-natal depression is seen in around 2-3% of women
- ☐ B. Puerperal psychosis has a recurrence rate of around 20%
- ☐ C. Baby-blues are seen in the majority of women
- ☐ D. Post-natal depression usually develops within the first month
- ☐ E. Sertraline can be used whilst mothers are breast feeding

Next question

Post-natal depression is seen in around 10% of women

### Post-partum mental health problems

Post-partum mental health problems range from the 'baby-blues' to puerperal psychosis

'Baby-blues'	Postnatal depression	Puerperal psychosis
Seen in around 60-70% of women	Affects around 10% of women	Affects approximately 0.2% of women
Typically seen 3-7 days following birth and is more common in primips	Most cases start within a month and typically peaks at 3 months	Onset usually within the first 2-3 weeks following birth
Mothers are characteristically anxious, tearful and irritable	Features are similar to depression seen in other circumstances	Features include severe swings in mood (similar to bipolar disorder) and disordered perception (e.g. auditory hallucinations)
Reassurance and support, the health visitor has a key role	As with the baby blues reassurance and support are important  Cognitive behavioural therapy may be beneficial. Certain SSRIs such as sertraline and paroxetine* may be used if symptoms are severe** - whilst they are secreted in breast milk it is not thought to be harmful to the infant	Admission to hospital is usually required  There is around a 20% risk of recurrence following future pregnancies

\*paroxetine is recommended by SIGN because of the low milk/plasma ratio

\*\*fluoxetine is best avoided due to a long half-life

A 65-year-old female with a history of ischaemic heart disease is noted to be depressed following a recent myocardial infarction. What would be the most appropriate antidepressant to start?

- |                       |                |
|-----------------------|----------------|
| <input type="radio"/> | A. Paroxetine  |
| <input type="radio"/> | B. Imipramine  |
| <input type="radio"/> | C. Flupentixol |
| <input type="radio"/> | D. Venlafaxine |
| <input type="radio"/> | E. Sertraline  |

[Next question](#)

Sertraline is the preferred antidepressant following a myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants

### Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are considered first-line treatment for the majority of patients with depression.

- citalopram and fluoxetine are currently the preferred SSRIs
- citalopram is useful for elderly patients as it is associated with lower risks of drug interactions
- sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants
- SSRIs should be used with caution in children and adolescents. Fluoxetine is the drug of choice when an antidepressant is indicated

### Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline are more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

### Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', but if given co-prescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above

- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

#### Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paraesthesia

A 35-year-old man with a history of schizophrenia is brought to the Emergency Department by worried friends due to drowsiness. On examination he is generally rigid. A diagnosis of neuroleptic malignant syndrome is suspected. Each one of the following is a feature of neuroleptic malignant syndrome, except:

<input type="radio"/>	A. Renal failure
<input type="radio"/>	B. Pyrexia
<input type="radio"/>	C. Elevated creatine kinase
<input type="radio"/>	D. Usually occurs after prolonged treatment
<input type="radio"/>	E. Tachycardia

[Next question](#)

Neuroleptic malignant syndrome is typically seen in patients who have just commenced treatment. Renal failure may occur secondary to rhabdomyolysis

### Neuroleptic malignant syndrome

Neuroleptic malignant syndrome is a rare but dangerous condition seen in patients taking antipsychotic medication. It carries a mortality of up to 10% and can also occur with atypical antipsychotics

#### Features

- more common in young male patients
- onset usually in first 10 days of treatment or after increasing dose
- pyrexia
- rigidity
- tachycardia

A raised creatine kinase is present in most cases. A leukocytosis may also be seen

#### Management

- stop antipsychotic
- IV fluids to prevent renal failure
- dantrolene may be useful in selected cases
- bromocriptine, dopamine agonist, may also be used

A 64-year-old woman presents as she is feeling down and sleeping poorly. After speaking to the patient and using a validated symptom measure you decide she has moderate depression. She has a past history of cerebrovascular disease and currently takes aspirin, ramipril and simvastatin. What is the most appropriate course of action?

- ☐ A. Stop aspirin, start citalopram
- ☐ B. Start venlafaxine
- ☐ C. Start citalopram + lansoprazole
- ☐ D. Stop aspirin, start clopidogrel + citalopram
- ☐ E. Start citalopram

[Next question](#)

SSRI + NSAID = GI bleeding risk - give a PPI

There is an increased incidence of gastrointestinal bleeding when aspirin / NSAIDs are combined with selective serotonin reuptake inhibitors. This patient should therefore also be offered a proton pump inhibitor such as lansoprazole. It would be inappropriate to stop aspirin in a patient with a history of cerebrovascular disease.

### Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are considered first-line treatment for the majority of patients with depression.

- citalopram and fluoxetine are currently the preferred SSRIs
- citalopram is useful for elderly patients as it is associated with lower risks of drug interactions
- sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants
- SSRIs should be used with caution in children and adolescents. Fluoxetine is the drug of choice when an antidepressant is indicated

### Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline are more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

## Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', but if given co-prescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

## Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paraesthesia



**Question 36 of 56**

Next

Which one of the following intervention is most likely to be beneficial in a patient with schizophrenia?

- |                       |                                  |
|-----------------------|----------------------------------|
| <input type="radio"/> | A. Counselling                   |
| <input type="radio"/> | B. Supportive psychotherapy      |
| <input type="radio"/> | C. Social skills training        |
| <input type="radio"/> | D. Adherence therapy             |
| <input type="radio"/> | E. Cognitive behavioural therapy |

Next question

**Schizophrenia: management**

NICE published guidelines on the management of schizophrenia in 2009.

Key points:

- oral atypical antipsychotics are first-line
- cognitive behavioural therapy should be offered to all patients
- close attention should be paid to cardiovascular risk-factor modification due to the high rates of cardiovascular disease in schizophrenic patients (linked to antipsychotic medication and high smoking rates)

**Question 37 of 56**

Next

A 69-year-old man is diagnosed as having Parkinson's disease. Which one of the following psychiatric problems is most likely to occur in this patient?

<input type="radio"/>	A. Tics
<input type="radio"/>	B. Psychosis
<input type="radio"/>	C. Mania
<input type="radio"/>	D. Dementia
<input type="radio"/>	E. Depression

Next question

Parkinson's disease - most common psychiatric problem is depression

Whilst dementia is common in patients with Parkinson's disease depression is known to exist in around 40%

**Parkinson's disease: features**

Parkinson's disease is a progressive neurodegenerative condition caused by degeneration of dopaminergic neurons in the substantia nigra.. This results in a classic triad of features: bradykinesia, tremor and rigidity. The symptoms of Parkinson's disease are characteristically asymmetrical

**Bradykinesia**

- poverty of movement also seen: mask-like facies
- difficulty in initiating movement

**Tremor**

- most marked at rest, 3-5 Hz
- typically 'pill-rolling'

**Rigidity**

- lead pipe
- cogwheel: due to superimposed tremor

**Other characteristic features**

- flexed posture
- short, shuffling steps

- micrographia
- drooling of saliva
- psychiatric features: depression is the most common feature (affects about 40%); dementia, psychosis and sleep disturbances may also occur
- impaired olfaction
- REM sleep behaviour disorder

**Drug-induced parkinsonism** has slightly different features to Parkinson's disease:

- motor symptoms are generally rapid onset and bilateral
- rigidity and rest tremor are uncommon

A patient with a history of depression presents for review. Which one of the following suggests an increased risk of suicide?

<input type="radio"/>	A. Being 25-years-old
<input checked="" type="radio"/>	B. History of arm cutting
<input type="radio"/>	C. Being married
<input type="radio"/>	D. Female sex
<input type="radio"/>	E. Having a busy job

[Next question](#)

Whilst arm cutting may sometimes be characterised as attention-seeking or 'releasing the pain' studies show that any history of deliberate self harm significantly increases the risk of suicide. Employment is a protective factor

### Suicide

Factors associated with risk of suicide following an episode of deliberate self harm:

- efforts to avoid discovery
- planning
- leaving a written note
- final acts such as sorting out finances
- violent method

These are in addition to standard risk factors for suicide

- male sex
- advancing age
- unemployment or social isolation
- divorced or widowed
- history of mental illness (depression, schizophrenia)
- history of deliberate self harm
- alcohol or drug misuse

A 31-year-old woman who gave birth two weeks ago presents for review with her husband. He is worried by her mood as she now seems depressed and is interacting poorly with the baby. He describes her mood three days ago being much different, when she was talking in a rapid and incoherent fashion about the future. The mother denies any hallucinations but states that her child has been brought into a 'very bad world'. What is the most appropriate management?

- ☐ A. Start fluoxetine
- ☐ B. Reassurance + review by health visitor
- ☐ C. Cognitive behavioural therapy
- ☐ D. Start lithium
- ☐ E. Arrange urgent admission

[Next question](#)

The mother may be suffering from puerperal psychosis and needs urgent admission to allow psychiatric evaluation

### Post-partum mental health problems

Post-partum mental health problems range from the 'baby-blues' to puerperal psychosis

'Baby-blues'	Postnatal depression	Puerperal psychosis
Seen in around 60-70% of women	Affects around 10% of women	Affects approximately 0.2% of women
Typically seen 3-7 days following birth and is more common in primips	Most cases start within a month and typically peaks at 3 months	Onset usually within the first 2-3 weeks following birth
Mothers are characteristically anxious, tearful and irritable	Features are similar to depression seen in other circumstances	Features include severe swings in mood (similar to bipolar disorder) and disordered perception (e.g. auditory hallucinations)
Reassurance and support, the health visitor has a key role	As with the baby blues reassurance and support are important  Cognitive behavioural therapy may be beneficial. Certain SSRIs such as sertraline and paroxetine* may be used if symptoms are severe** - whilst they are secreted in breast milk it is not thought to be harmful to the infant	Admission to hospital is usually required  There is around a 20% risk of recurrence following future pregnancies

\*paroxetine is recommended by SIGN because of the low milk/plasma ratio

\*\*fluoxetine is best avoided due to a long half-life

A 36-year-old patient presents with nausea, headaches and palpitations. He has had multiple previous admissions with such symptoms over the past 2 years, each time no organic cause was found. What kind of disorder is this likely to represent?

<input type="radio"/>	A. Munchausen's syndrome
<input type="radio"/>	B. Hypochondrial disorder
<input type="radio"/>	C. Somatisation disorder
<input type="radio"/>	D. Conversion disorder
<input type="radio"/>	E. Dissociative disorder

[Next question](#)

### Unexplained symptoms

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

#### Somatisation disorder

- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

#### Hypochondrial disorder

- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

#### Conversion disorder

- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
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#### Dissociative disorder

- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor

- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

#### Munchausen's syndrome

- also known as factitious disorder
- the intentional production of physical or psychological symptoms

#### Malingering

- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

**Question 41 of 56**

Next

The risk of developing schizophrenia if one monozygotic twin is affected is approximately:

<input type="radio"/>	A. 10%
<input type="radio"/>	B. 20%
<input type="radio"/>	C. 50%
<input type="radio"/>	D. 75%
<input type="radio"/>	E. >95%

Next question

**Schizophrenia: epidemiology**

Risk of developing schizophrenia

- monozygotic twin has schizophrenia = 50%
- parent has schizophrenia = 10-15%
- sibling has schizophrenia = 10%
- no relatives with schizophrenia = 1%



**Question 42 of 56**

Next

A 43-year-old man with a history of schizophrenia is taken off chlorpromazine due to troublesome parkinsonian symptoms. Which one of the following atypical antipsychotic is it least suitable for him to be commenced on as the next step?

- |                       |                |
|-----------------------|----------------|
| <input type="radio"/> | A. Quetiapine  |
| <input type="radio"/> | B. Amisulpride |
| <input type="radio"/> | C. Olanzapine  |
| <input type="radio"/> | D. Risperidone |
| <input type="radio"/> | E. Clozapine   |

Next question

Clozapine is no longer used first-line due to the risk of agranulocytosis

**Atypical antipsychotics**

Atypical antipsychotics should now be used first-line in patients with schizophrenia, according to 2005 NICE guidelines. The main advantage of the atypical agents is a significant reduction in extra-pyramidal side-effects.

Adverse effects of atypical antipsychotics

- weight gain
- clozapine is associated with agranulocytosis (see below)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:

- increased risk of stroke (especially olanzapine and risperidone)
- increased risk of venous thromboembolism

Examples of atypical antipsychotics

- clozapine
- olanzapine
- risperidone
- quetiapine
- amisulpride

Clozapine, one of the first atypical agents to be developed, carries a significant risk of agranulocytosis and full blood count monitoring is therefore essential during treatment. For this reason clozapine should only be used in patients resistant to other antipsychotic medication

#### Adverse effects of clozapine

- agranulocytosis (1%), neutropaenia (3%)
- reduced seizure threshold - can induce seizures in up to 3% of patients

Which one of the following statements regarding cognitive behavioural therapy is incorrect?

<input type="radio"/>	A. May be useful in the management of generalised anxiety disorder
<input type="radio"/>	B. Can be used for patients already taking antidepressants
<input type="radio"/>	C. Usually consists of one to two hour sessions once per week
<input type="radio"/>	D. Should be completed within 6 months
<input type="radio"/>	E. Patients usually get around 35-40 hours in total

Next question

### Cognitive behavioural therapy

Main points

- useful in the management of depression and anxiety disorders
- usually consists of one to two hour sessions once per week
- should be completed within 6 months
- patients usually get around 16-20 hours in total

A patient reports feeling unwell after suddenly stopping paroxetine. Which one of the following symptoms is most consistent with selective serotonin reuptake inhibitor discontinuation syndrome?

<input type="radio"/>	A. Postural hypotension
<input type="radio"/>	B. Diarrhoea
<input type="radio"/>	C. Myoclonic jerks
<input type="radio"/>	D. Hallucinations
<input type="radio"/>	E. Seizures

[Next question](#)

Selective serotonin reuptake inhibitor discontinuation syndrome can present with a wide variety of symptoms including diarrhoea, vomiting and abdominal pain.

### Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are considered first-line treatment for the majority of patients with depression.

- citalopram and fluoxetine are currently the preferred SSRIs
- citalopram is useful for elderly patients as it is associated with lower risks of drug interactions
- sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants
- SSRIs should be used with caution in children and adolescents. Fluoxetine is the drug of choice when an antidepressant is indicated

### Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline are more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

### Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', but if given co-prescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above

- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

#### Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paraesthesia

A 42-year-old woman presents for review. Her husband reports that she has had an argument with their son which resulted in him leaving home. Since this happened she has not been able to speak. Clinical examination of her throat and chest is unremarkable. Which one of the following terms best describes this presentation?

<input type="radio"/>	A. Aprrosodia
<input type="radio"/>	B. Schizophasia
<input type="radio"/>	C. Expressive aphasia
<input type="radio"/>	D. Akinetic mutism
<input type="radio"/>	E. Psychogenic aphonia

[Next question](#)

Psychogenic aphonia is considered to be a form of conversion disorder. Please see the link for more details.

### Aphonia

Aphonia describes the inability to speak. Causes include:

- recurrent laryngeal nerve palsy (e.g. Post-thyroidectomy)
- psychogenic

Which one of the following is least recognised as a potential adverse effect of electroconvulsive therapy?

<input type="radio"/>	A. Nausea
<input type="radio"/>	B. Epilepsy
<input type="radio"/>	C. Cardiac arrhythmias
<input type="radio"/>	D. Short term memory impairment
<input type="radio"/>	E. Headache

Next question

Although electroconvulsive therapy, by definition, causes a controlled seizure there is no increased risk of epilepsy in the long-term.

### Electroconvulsive therapy

Electroconvulsive therapy is a useful treatment option for patients with severe depression refractory to medication or those with psychotic symptoms. The only absolute contraindications is raised intracranial pressure.

#### Short-term side-effects

- headache
- nausea
- short term memory impairment
- memory loss of events prior to ECT
- cardiac arrhythmia

#### Long-term side-effects

- some patients report impaired memory

A 24-year-old man is brought to the Emergency Department by his brother who is concerned about his odd behaviour. Over the past two weeks he has started to tell his brother that he can hear people talking about him on the radio. He denies any auditory hallucinations. During the consultation he scores 10/10 on the mini-mental state examination. When asked to explain the meaning of the statement 'people in glass houses shouldn't throw stones' he replies 'you may break the glass'. What is this an example of?

- |                       |                        |
|-----------------------|------------------------|
| <input type="radio"/> | A. Depression          |
| <input type="radio"/> | B. Autistic thinking   |
| <input type="radio"/> | C. Concrete thinking   |
| <input type="radio"/> | D. Delusional disorder |
| <input type="radio"/> | E. Acute mania         |

[Next question](#)

This is an example of concrete thinking where a patient cannot use abstraction to understand the meaning of a sentence. It is more common in schizophrenia. Literal thinking is of course a feature of autism but this would not explain his delusional perception and is unlikely to present in a sub-acute fashion at this age

### Schizophrenia: features

Schneider's first rank symptoms may be divided into auditory hallucinations, thought disorders, passivity phenomena and delusional perceptions:

Auditory hallucinations of a specific type:

- two or more voices discussing the patient in the third person
- thought echo
- voices commenting on the patient's behaviour

Thought disorder\*:

- thought insertion
- thought withdrawal
- thought broadcasting

Passivity phenomena:

- bodily sensations being controlled by external influence
- actions/impulses/feelings - experiences which are imposed on the individual or influenced by others

Delusional perceptions



- a two stage process) where first a normal object is perceived then secondly there is a sudden intense delusional insight into the objects meaning for the patient e.g. 'The traffic light is green therefore I am the King'.

Other features of schizophrenia include

- impaired insight
- incongruity/blunting of affect (inappropriate emotion for circumstances)
- decreased speech
- neologisms: made-up words
- catatonia
- negative symptoms: incongruity/blunting of affect, anhedonia (inability to derive pleasure), alogia (poverty of speech), avolition (poor motivation)

\*occasionally referred to as thought alienation

**Question 48 of 56**

Next

A 16-year-old girl is brought for review by her father. She is talented violinist and is due to start music college in a few weeks time. Her parents are concerned she has had a stroke as she is reporting weakness on her right side. Neurological examination is inconsistent and you suspect a non-organic cause for her symptoms. Despite reassurance about the normal examination findings the girl remains unable to move her right arm. What is the most appropriate term for this behaviour?

<input type="radio"/>	A. Hypochondrial disorder
<input type="radio"/>	B. Munchausen's syndrome
<input type="radio"/>	C. Somatisation disorder
<input checked="" type="radio"/>	D. Conversion disorder
<input type="radio"/>	E. Munchausen's-by-proxy syndrome

Next question

This is a typical conversion disorder. There may be underlying tension regarding her musical career which be manifesting itself as apparent limb weakness.

**Unexplained symptoms**

There are a wide variety of psychiatric terms for patients who have symptoms for which no organic cause can be found:

**Somatisation disorder**

- multiple physical SYMPTOMS present for at least 2 years
- patient refuses to accept reassurance or negative test results

**Hypochondrial disorder**

- persistent belief in the presence of an underlying serious DISEASE, e.g. cancer
- patient again refuses to accept reassurance or negative test results

**Conversion disorder**

- typically involves loss of motor or sensory function
- the patient doesn't consciously feign the symptoms (factitious disorder) or seek material gain (malingering)
- patients may be indifferent to their apparent disorder - la belle indifference - although this has not been backed up by some studies

**Dissociative disorder**

- dissociation is a process of 'separating off' certain memories from normal consciousness
- in contrast to conversion disorder involves psychiatric symptoms e.g. Amnesia, fugue, stupor
- dissociative identity disorder (DID) is the new term for multiple personality disorder as is the most severe form of dissociative disorder

#### Munchausen's syndrome

- also known as factitious disorder
- the intentional production of physical or psychological symptoms

#### Malingering

- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

Which one of the following selective serotonin reuptake inhibitors has the highest incidence of discontinuation symptoms?

<input type="radio"/>	A. Paroxetine
<input type="radio"/>	B. Citalopram
<input type="radio"/>	C. Escitalopram
<input type="radio"/>	D. Fluoxetine
<input type="radio"/>	E. Sertraline

[Next question](#)

Paroxetine - higher incidence of discontinuation symptoms

### Depression: selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are considered first-line treatment for the majority of patients with depression.

- citalopram and fluoxetine are currently the preferred SSRIs
- citalopram is useful for elderly patients as it is associated with lower risks of drug interactions
- sertraline is useful post myocardial infarction as there is more evidence for its safe use in this situation than other antidepressants
- SSRIs should be used with caution in children and adolescents. Fluoxetine is the drug of choice when an antidepressant is indicated

### Adverse effects

- gastrointestinal symptoms are the most common side-effect
- there is an increased risk of gastrointestinal bleeding in patients taking SSRIs. A proton pump inhibitor should be prescribed if a patient is also taking a NSAID
- patients should be counselled to be vigilant for increased anxiety and agitation after starting a SSRI
- fluoxetine and paroxetine have a higher propensity for drug interactions
- citalopram and sertraline are more suitable for patients with chronic physical health problems as they have a lower propensity for drug interactions.

## Interactions

- NSAIDs: NICE guidelines advise 'do not normally offer SSRIs', but if given co-prescribe a proton pump inhibitor
- warfarin / heparin: NICE guidelines recommend avoiding SSRIs and considering mirtazapine
- aspirin: see above
- triptans: avoid SSRIs

Following the initiation of antidepressant therapy patients should normally be reviewed by a doctor after 2 weeks. For patients under the age of 30 years or at increased risk of suicide they should be reviewed after 1 week. If a patient makes a good response to antidepressant therapy they should continue on treatment for at least 6 months after remission as this reduces the risk of relapse.

When stopping a SSRI the dose should be gradually reduced over a 4 week period (this is not necessary with fluoxetine). Paroxetine has a higher incidence of discontinuation symptoms.

## Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paraesthesia

**Question 50 of 56**

Next

You review a 55-year-old woman who has become dependant on temazepam, which was initially prescribed as a hypnotic. She is keen to end her addiction to temazepam and asks for help. Her current dose is 20mg on. What is the most appropriate strategy?

- |                       |   |
|-----------------------|---|
| <input type="radio"/> | A. Switch to the equivalent zopiclone dose then slowly withdraw over the next 2 weeks         |
| <input type="radio"/> | B. Switch to the equivalent diazepam dose then slowly withdraw over the next 2 weeks          |
| <input type="radio"/> | C. Switch to the equivalent zopiclone dose then slowly withdraw over the next 2 months        |
| <input type="radio"/> | D. Switch to the equivalent chlordiazepoxide dose then slowly withdraw over the next 2 months |
| <input type="radio"/> | E. Switch to the equivalent diazepam dose then slowly withdraw over the next 2 months         |

Next question

**Benzodiazepines**

Benzodiazepines enhance the effect of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). They therefore are used for a variety of purposes:

- sedation
- hypnotic
- anxiolytic
- anticonvulsant
- muscle relaxant

Patients commonly develop a tolerance and dependence to benzodiazepines and care should therefore be exercised on prescribing these drugs. The Committee on Safety of Medicines advises that benzodiazepines are only prescribed for a short period of time (2-4 weeks).

The BNF gives advice on how to withdraw a benzodiazepine. The dose should be withdrawn in steps of about 1/8 (range 1/10 to 1/4) of the daily dose every fortnight. A suggested protocol for patients experiencing difficulty is given:

- switch patients to the equivalent dose of diazepam
- reduce dose of diazepam every 2-3 weeks in steps of 2 or 2.5 mg
- time needed for withdrawal can vary from 4 weeks to a year or more

If patients withdraw too quickly from benzodiazepines they may experience benzodiazepine withdrawal

syndrome, a condition very similar to alcohol withdrawal syndrome. This may occur up to 3 weeks after stopping a long-acting drug. Features include:

- insomnia
- irritability
- anxiety
- tremor
- loss of appetite
- tinnitus
- perspiration
- perceptual disturbances
- seizures

A 34-year-old ex-soldier with a history of post-traumatic stress disorder returns for review. He has had a course of eye movement desensitisation and reprocessing therapy which was not helpful and is reluctant to try cognitive behavioural therapy. Of the options listed, which medication may be useful in such patients?

- |                       |                |
|-----------------------|----------------|
| <input type="radio"/> | A. Fluoxetine  |
| <input type="radio"/> | B. Citalopram  |
| <input type="radio"/> | C. Mirtazapine |
| <input type="radio"/> | D. Topiramate  |
| <input type="radio"/> | E. Bupropion   |

Next question

### Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) can develop in people of any age following a traumatic event, for example a major disaster or childhood sexual abuse. It encompasses what became known as 'shell shock' following the first world war. One of the DSM-IV diagnostic criteria is that symptoms have been present for more than one month

#### Features

- re-experiencing: flashbacks, nightmares, repetitive and distressing intrusive images
- avoidance: avoiding people, situations or circumstances resembling or associated with the event
- hyperarousal: hypervigilance for threat, exaggerated startle response, sleep problems, irritability and difficulty concentrating
- emotional numbing - lack of ability to experience feelings, feeling detached

#### from other people

- depression
- drug or alcohol misuse
- anger
- unexplained physical symptoms

#### Management

- following a traumatic event single-session interventions (often referred to as debriefing) are not recommended
- watchful waiting may be used for mild symptoms lasting less than 4 weeks
- military personnel have access to treatment provided by the armed forces
- trauma-focused cognitive behavioural therapy (CBT) or eye movement desensitisation and reprocessing (EMDR) therapy may be used in more severe cases
- drug treatments for PTSD should not be used as a routine first-line treatment for adults. If drug treatment is used then paroxetine or mirtazapine are recommended



Which of the following types of tricyclic antidepressant is considered the safest in overdose?

- ☐ A. Nortriptyline
- ☐ B. Imipramine
- ☐ C. Dosulepin
- ☐ D. Lofepramine
- ☐ E. Clomipramine

Next question

Lofepramine - the safest TCA in overdose

### Tricyclic antidepressants

Tricyclic antidepressants (TCAs) are used less commonly now for depression due to their side-effects and toxicity in overdose. They are however used widely in the treatment of neuropathic pain, where smaller doses are typically required.

#### Common side-effects

- drowsiness
- dry mouth
- blurred vision
- constipation
- urinary retention

#### Choice of tricyclic

- low-dose amitriptyline is commonly used in the management of neuropathic pain and the prophylaxis of headache (both tension and migraine)
- lofepramine has a lower incidence of toxicity in overdose
- amitriptyline and dosulepin (dothiepin) are considered the most dangerous in overdose

More sedative	Less sedative
Amitriptyline	Imipramine
Clomipramine	Lofepramine
Dosulepin	Nortriptyline
Trazodone*	

\*trazodone is technically a 'tricyclic-related antidepressant'

A 46-year-old man is seen by an occupation health doctor due to long-term sickness leave. He states chronic lower back pain prevents him from working but examination findings are inconsistent and the doctor suspects a non-organic cause of his symptoms. This is an example of a:

<input type="radio"/>	A. Conversion disorder
<input type="radio"/>	B. Munchausen's syndrome
<input type="radio"/>	C. Malingering
<input type="radio"/>	D. Hypochondrial disorder
<input type="radio"/>	E. Somatisation disorder

[Next question](#)

### Unexplained symptoms

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#### Munchausen's syndrome

- also known as factitious disorder
- the intentional production of physical or psychological symptoms

#### Malingering

- fraudulent simulation or exaggeration of symptoms with the intention of financial or other gain

You are considering prescribing a selective serotonin reuptake inhibitor for a patient with depression. Which class of drug is most likely to interact with a selective serotonin reuptake inhibitor?

- |                       |                       |
|-----------------------|-----------------------|
| <input type="radio"/> | A. Beta-blocker       |
| <input type="radio"/> | B. Thiazolidinediones |
| <input type="radio"/> | C. Tetracycline       |
| <input type="radio"/> | D. Statin             |
| <input type="radio"/> | E. Triptan            |

[Next question](#)

### Depression: selective serotonin reuptake inhibitors

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#### Discontinuation symptoms

- increased mood change
- restlessness
- difficulty sleeping
- unsteadiness
- sweating
- gastrointestinal symptoms: pain, cramping, diarrhoea, vomiting
- paraesthesia

Which class of drug have the Medicines and Healthcare products Regulatory Agency warned may be associated with an increased risk of venous thromboembolism in elderly patients?

<input type="radio"/>	A. Tricyclic antidepressants
<input type="radio"/>	B. 5HT3 antagonists
<input type="radio"/>	C. Third generation cephalosporins
<input type="radio"/>	D. Benzodiazepines
<input type="radio"/>	E. Atypical antipsychotics

[Next question](#)

Antipsychotics in the elderly - increased risk of stroke and VTE

## Antipsychotics

Antipsychotics act as dopamine D2 receptor antagonists, blocking dopaminergic transmission in the mesolimbic pathways. Conventional antipsychotics are associated with problematic extrapyramidal side-effects which has led to the development of atypical antipsychotics such as clozapine

### Extrapyramidal side-effects

- Parkinsonism
- acute dystonia (e.g. torticollis, oculogyric crisis)
- akathisia (severe restlessness)
- tardive dyskinesia (late onset of choreoathetoid movements, abnormal, involuntary, may occur in 40% of patients, may be irreversible, most common is chewing and pouting of jaw)

The Medicines and Healthcare products Regulatory Agency has issued specific warnings when antipsychotics are used in elderly patients:

- increased risk of stroke
- increased risk of venous thromboembolism

### Other side-effects

- antimuscarinic: dry mouth, blurred vision, urinary retention, constipation
- sedation, weight gain
- raised prolactin: galactorrhoea
- neuroleptic malignant syndrome: pyrexia, muscle stiffness
- reduced seizure threshold (greater with atypicals)

### Question 56 of 56

A patient presents three days after suddenly stopping diazepam after having taken it for over two years. He feels generally unwell. Which one of the following features would suggest a diagnosis other than benzodiazepine withdrawal syndrome?

<input type="radio"/>	A. Hypothermia
<input type="radio"/>	B. Loss of appetite
<input type="radio"/>	C. Tinnitus
<input type="radio"/>	D. Perceptual disturbances
<input type="radio"/>	E. Perspiration

Hypothermia is not a feature of benzodiazepine withdrawal syndrome.

### Benzodiazepines

Benzodiazepines enhance the effect of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA). They therefore are used for a variety of purposes:

- sedation
- hypnotic
- anxiolytic
- anticonvulsant
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- insomnia
- irritability

- anxiety
- tremor
- loss of appetite
- tinnitus
- perspiration
- perceptual disturbances
- seizures



# Reference ranges

Reference ranges vary according to individual labs. All values are for adults unless otherwise stated

## Full blood count

Haemoglobin	Men: 13.5-18 g/dl Women: 11.5-16 g/dl
Mean cell volume	82-100 fl
Platelets	150-400 * 10 <sup>9</sup> /l
White blood cells	4-11 * 10 <sup>9</sup> /l

## Urea and electrolytes

Sodium	135-145 mmol/l
Potassium	3.5 - 5.0 mmol/l
Urea	2.0-7 mmol/l
Creatinine	55-120 umol/l
Bicarbonate	22-28 mmol/l

## Liver function tests

Bilirubin	3-17 umol/l
Alanine transferase (ALT)	3-40 iu/l
Aspartate transaminase (AST)	3-30 iu/l
Alkaline phosphatase (ALP)	30-100 umol/l
Gamma glutamyl transferase (yGT)	8-60 u/l
Albumin	35-50 g/l
Total protein	60-80 g/l

## Other haematology

Erythrocyte sedimentation rate (ESR)	Men: < (age / 2) mm/hr Women: < ((age + 10) / 2) mm/hr
Prothrombin time (PT)	10-14 secs
Activated partial thromboplastin time (APTT)	25-35 secs
Ferritin	20-230 ng/ml
Vitamin B12	200-900 ng/l
Folate	3.0 nmol/l
Reticulocytes	0.5-1.5%

## Other biochemistry

Calcium	2.1-2.6 mmol/l

Phosphate	0.8-1.4 mmol/l
CRP	< 10 mg/l
Thyroid stimulating hormone (TSH)	0.5-5.5 mu/l
Free thyroxine (T4)	9-22 pmol/l
Total thyroxine (T4)	70-140 nmol/l
Amylase	70-300 u/l
Uric acid	0.18-0.48 mmol/l

## Arterial blood gases

pH	7.35 - 7.45
pCO2	4.5 - 6.0 kPa
pO2	10 - 14 kPa

## Lipids

Desirable lipid values depend on other risk factors for cardiovascular disease, below is just a guide:

Total cholesterol	< 5 mmol/l
Triglycerides	< 2 mmol/l
HDL cholesterol	> 1 mmol/l
LDL cholesterol	< 3 mmol/l